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E#      FILE              FREQUENCY  TERM
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E1      USPAT                    1    JUTERBOCK, KARSTEN/IN
E2      USPAT                    1    JUTIER, PIERRE/IN
E3      USPAT                    0 --> JUTILA/IN
E4      USPAT                    1    JUTILA, PENTTI K/IN
E5      USPAT                    1    JUTILA, RAYMOND E/IN
E6      USPAT                    2    JUTILA, RAYMOND EINO/IN
E7      USPAT                    1    JUTKEVICH, VALERY I/IN
E8      USPAT                    1    JUTKEVICH, VALERY IVANOVICH/IN
E9      USPAT                    1    JUTO, YASURO/IN
E10     USPAT                    1    JUTRAS, GILLES/IN
E11     USPAT                    1    JUTRAS, GUY F/IN
E12     USPAT                    1    JUTRAS, MARIO/IN
=> s (e(w)selectin? or elam) and (l(w)selectin) or ((leucocyte or
leukocyte)(w)adhesion(w)molecule)
       1196709 E
        168611 SELECTIN?

          1039 E(W)SELECTIN?
           170 ELAM
        464582 L
            88 SELECTIN
            23 L(W)SELECTIN
           582 LEUCOCYTE
          2719 LEUKOCYTE
         90533 ADHESION
         93731 MOLECULE
            62 (LEUCOCYTE OR LEUKOCYTE)(W)ADHESION(W)MOLECULE
L1          74 (E(W)SELECTIN? OR ELAM) AND (L(W)SELECTIN) OR ((LEUCOCYTE O
R L
               EUKOCYTE)(W)ADHESION(W)MOLECULE)
=> s l1 and common(w)epitope?
        544684 COMMON
          2778 EPITOPE?
           110 COMMON(W)EPITOPE?
L2           0 L1 AND COMMON(W)EPITOPE?
=> s (e(w)selectin? or elam)(p)(l(w)selectin)
       1196709 E
        168611 SELECTIN?

           170 ELAM
        464582 L
            88 SELECTIN

L3          23 (E(W)SELECTIN? OR ELAM)(P)(L(W)SELECTIN)
=> d l3 1-23

1.  5,541,287, Jul. 30, 1996, Pretargeting methods and compounds; Eric K.
Yau, et al., 530/317, 323, 330, 331, 332, 345 [IMAGE AVAILABLE]

2.  5,527,890, Jun. 18, 1996, Derivatives of triterpenoid acids and uses
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thereof; Narasinga Rao, et al., 536/5; 424/533; 536/4.1, 4.4, 17.2, 17.4, 17.9, 18.7 [IMAGE AVAILABLE]

3. 5,527,785, Jun. 18, 1996, Selectin receptor modulating compositions; Michael P. Bevilacqua, et al., 514/56, 54, 61; 536/21 [IMAGE AVAILABLE]

4. 5,519,008, May 21, 1996, Derivatives of triterpenoid acids as inhibitors of cell-adhesion molecules **ELAM**-1 (**E**-**selectin**) and LECAM-1 (**L**-**selectin**); Narasinga Rao, et al., 514/26, 2, 25, 53, 54, 61, 563; 536/5, 17.2, 17.3, 17.4, 17.5, 17.6, 18.1, 22.1, 55, 55.1; 552/502 [IMAGE AVAILABLE]

5. 5,508,387, Apr. 16, 1996, Selectin binding glycopeptides; Peng C. Tang, et al., 530/403, 322; 536/18.7, 53, 54, 115 [IMAGE AVAILABLE]

6. 5,494,790, Feb. 27, 1996, .alpha.-3 sialyltransferase; Katsutoshi Sasaki, et al., 435/6, 85, 193, 252.33, 320.1; 536/23.2 [IMAGE AVAILABLE]

7. 5,489,578, Feb. 6, 1996, Sulfated ligands for l-selectin and methods of treating inflammation; Steven D. Rosen, et al., 514/61, 25, 53, 54, 62; 536/4.1, 17.2, 18.7, 53, 54, 55, 55.1, 55.2 [IMAGE AVAILABLE]

8. 5,486,536, Jan. 23, 1996, Sulfatides as anti-inflammatory compounds; Peter A. Ward, et al., 514/460 [IMAGE AVAILABLE]

9. 5,484,891, Jan. 16, 1996, Selectin ligands; Laurence A. Lasky, et al., 530/387.3; 435/7.2; 530/350, 395 [IMAGE AVAILABLE]

10. 5,470,843, Nov. 28, 1995, Carbohydrate-containing polymers, their preparation and use; Wilhelm Stahl, et al., 514/61, 25, 54, 55, 56, 60; 525/32.2; 536/4.1, 17.2, 18.5, 18.7, 20, 21, 45, 102, 124 [IMAGE AVAILABLE]

11. 5,464,935, Nov. 7, 1995, Peptide inhibitors of selectin binding; George A. Heavner, et al., 530/329, 330 [IMAGE AVAILABLE]

12. 5,464,815, Nov. 7, 1995, Inhibition of heparin-binding; Steven Chamow, et al., 514/8; 424/85.2; 436/86, 87; 514/21; 530/412 [IMAGE AVAILABLE]

13. 5,464,778, Nov. 7, 1995, Glycoprotein ligand for P-selectin and methods of use thereof; Richard D. Cummings, et al., 436/503; 435/7.1, 7.24; 436/501; 536/53, 55.1, 55.2, 123.1 [IMAGE AVAILABLE]

14. 5,460,945, Oct. 24, 1995, Device and method for analysis of blood components and identifying inhibitors and promoters of the inflammatory response; Timothy A. Springer, et al., 435/7.24; 422/58, 69; 427/2.11, 2.13; 435/2, 7.23, 7.8, 29, 30, 174, 176, 177, 240.2, 287.1, 287.2, 287.9, 288.3, 288.5 [IMAGE AVAILABLE]

15. 5,444,050, Aug. 22, 1995, Binding of E-selectin or P-selectin to sialyl Lewis.sup.x or sialyl-Lewis.sup.a; Timothy P. Kogan, et al., 514/25; 536/17.2, 17.3, 17.4, 17.5, 18.4 [IMAGE AVAILABLE]

16. 5,440,015, Aug. 8, 1995, Selectin peptide medicaments for treating disease; Bruce A. Macher, et al., 530/329, 328 [IMAGE AVAILABLE]

17. 5,426,113, Jun. 20, 1995, Method of preventing ulcer formation

caused by nonsteroidal antiinflammatory drugs employing tetrazol-benzothiophene carboxamide compounds; Joseph E. Low, 514/381, 382, 444 [IMAGE AVAILABLE]

18. 5,418,147, May 23, 1995, Glycosyl-phosphatidylinositol-specific phospholipase D; Kuo-Sen Huang, et al., 435/69.1, 68.1, 69.7, 69.8, 198, 252.3, 320.1; 536/23.2, 23.4; 935/47, 48 [IMAGE AVAILABLE]

19. 5,412,123, May 2, 1995, Anthraquinone and anthracene derivatives as inhibitors of the cell-adhesion molecules of the immune system; Narasinga Rao, et al., 552/209; 549/426, 427; 552/234, 236, 240, 242, 243, 262 [IMAGE AVAILABLE]

20. 5,389,520, Feb. 14, 1995, Specific detection of cell surface receptor leukocyte adhesion molecule-1; Thomas F. Tedder, et al., 435/7.24, 2, 240.2; 436/548 [IMAGE AVAILABLE]

21. 5,384,249, Jan. 24, 1995, .alpha.2.fwdarw.3 sialyltransferase; Katsutoshi Sasaki, et al., 435/68.1, 85, 193 [IMAGE AVAILABLE]

22. 5,360,733, Nov. 1, 1994, Human .beta.1-6 n-acetylglucosaminyl transferase; Minoru Fukuda, et al., 435/193, 69.7, 97 [IMAGE AVAILABLE]

23. 5,304,640, Apr. 19, 1994, DNA sequence encoding a selectin ligand; Laurence A. Lasky, et al., 536/23.5; 435/69.1, 172.3, 240.2, 320.1 [IMAGE AVAILABLE]

=> d l3 1-23 kwic

US PAT NO: 5,541,287 [IMAGE AVAILABLE] L3: 1 of 23

DETDESC:

DETD(42)

Other . . . anti-tumor agents include cytokines, such as IL-2, tumor necrosis factor or the like, lectin inflammatory response promoters (selectins), such as **L**-**selectin**, **E**-**selectin**, P-selectin or the like, and like molecules.

US PAT NO: 5,527,890 [IMAGE AVAILABLE] L3: 2 of 23

SUMMARY:

BSUM(7)

A . . . (hereinafter LEC-CAMs) in certain diseases including cancer, arthritis, and in the inflammatory response. The three known members of this family, **L**-**Selectin** (LECAM-1, LAM-1, gp90MEL), **E**-**Selectin** (LECAM-2, **ELAM**-1) and P-Selectin (LECAM-3, GMP-140, PADGEM), each contain a domain with homology to the calcium-dependent lectins (C-lectins), an EGF-like domain, and. . . Cell (1989) 56:1045-1055; Tedder et al., J. Exp. Med. (1989) 170:123-133). Perhaps the most studied of the three selectins is **E**-**selectin** which is present on stimulated vascular endothelium, and is involved in neutrophil attachment prior to extravasation during an inflammatory response.. . .

US PAT NO: 5,527,785 [IMAGE AVAILABLE] L3: 3 of 23

SUMMARY:

BSUM(6)

The . . . a group of CAMs which are named for the cell type on which they were originally identified. The selectins include **E**-**selectin** (endothelial cells), P-selectin (platelets and endothelial cells) and **L**-**selectin** (lymphocytes).

SUMMARY:

BSUM(7)

The . . . (e.g., ICAM-1, vascular cell adhesion molecule-1 and the leukocyte integrins) to effect adhesive interactions of leukocytes, platelets and endothelial cells. **E**-**selectin** was first shown to support the adhesion of neutrophils to cytokine-activated endothelium (Bevilacqua, et al., Proc. Natl. Acad. Sci., USA. 84:9238, 1987; Bevilacqua, et al., Science 243:1160, 1989). Subsequent studies in vitro have suggested that **E**-**selectin** also supports the binding of monocytes, a sub-population of memory T lymphocytes, eosinophils and basophils. Similarly, P-selectin also supports leukocyte adhesion. In addition to its role in lymphocyte homing, **L**-**selectin** appears to participate in the adhesion of neutrophils, monocytes and lymphocytes to activated endothelium (reviewed in Bevilacqua, M. and Nelson,. . .

SUMMARY:

BSUM(8)

Selectins . . . 63:467, 1990). Other studies identified the sylated form of this oligosaccharide, sLe.sup.x (Neu5Ac.alpha.2-3Gal.beta.1-4(Fuc.alpha.1-3)GIcNAc) and/or closely related structures as ligands of **E**-**selectin**. sLe.sup.x and other fucosylated lactosamines are found in abundance on circulating neutrophils and monocytes and on a small percentage of. . . P-selectin ligands, and that oligosaccharides containing sLe.sup.x are recognized by this molecule. In addition, human E- and P-selectin and murine **L**-**selectin** have been shown to interact with molecules containing sLe.sup.a (Neu5Ac.alpha.2-3Gal.beta.1-3(Fuc.alpha.1-4)GIcNAc), a structural isomer of sLe.sup.x. sLe.sup.a is not typically expressed. . .

SUMMARY:

BSUM(9)

In . . . from storage granules to the surface within minutes. In response to endotoxin, IL-1, or TNF, endothelial cells biosynthesize and express **E**-**selectin** as well as VCAM-1 and ICAM-1 over a period of hours to days. **L**-**selectin** is constitutively expressed by leukocytes and appears to recognize a cytokine-induced endothelial cell surface ligand. Inflammatory processes are essential for. . .

DETDESC:

DETD(25)

FIG. . . . Publishing Associates and Wiley-Interscience, 1991, New York, N.Y.) with cDNA encoding full length P-selectin Johnston, et al., Cell 56:1033-1044, 1989. **L**-**selectin** (Siegelman, M. H., et al., Science, 243:1165-1172, 1989; Lasky, L. A., et al., Cell, 56:1045-1055, 1989) or **E**-**selectin** (Bevilacqua, M. P., et al., Science, 243:1160-1165, 1989). Tetrasaccharide and hexasaccharide fragments of heparin blocked the adhesion of HL60 cells to COS cells transfected with cDNAs encoding P- or **L**-**selectin**, but not **E**-**selectin**. In addition, these heparin fragments blocked the adhesion of human polymorphonuclear leukocytes (PMNs, neutrophils) to P-COS, but not to E-COS. . . and Anderson, B. R., J. Immunol. Methods, 5:249-254, 1974). Isolated PMN were incubated with COS cells transfected with P- or **E**-**selectin** cDNAs. Carbohydrates or antibodies were added to the COS cells 30 minutes prior to addition of PMNs to achieve a final concentration of 1 mg/ml. The blocking monoclonal antibodies were G1 (P-selectin) (R. McEver, University of Oklahoma) and H18/7 (**E**-**selectin**) (University of California, San Diego). A trisulfated disaccharide fragment of heparin (.alpha..DELTA.UA-2S[1-4]GIcNS-6S) had little blocking activity at the concentrations tested in these adhesion assays, but was somewhat effective in the competition ELISA on **L**-**selectin** (see below).

DETDESC:

DETD(26)

The . . . line, LS180, is a useful model for studying selectin-dependent adhesion since it binds to all three selectins. E-, P-, and **L**-**selectin**-Ig were immobilized on microwell (Terasaki) plates coated with protein A. Five .mu.l of buffer containing crude heparin, di-, tetra- or. . . shows that hexasaccharide and tetrasaccharide fragments of heparin inhibited the adhesion of LS180 cells to plates coated with P- and **L**-**selectin**-Ig, but not **E**-**selectin**-Ig. The heparin disaccharide had no effect at the same concentration based on weight (a two-fold higher molar concentration compared to. . .

DETDESC:

DETD(28)

The . . . to reduce binding to 50% of maximum) allows comparison of relative blocking activity. Although heparin fragments had no effect on **E**-**selectin**-Ig binding to BSA-sLe.sup.x at concentrations up to 1 mg/ml (FIG. 6), tetrasaccharide and hexasaccharide, fragments of heparin inhibited the binding of P- and **L**-**selectin** Ig to plates coated with BSA-sLe.sup.x (FIGS. 7 and 8). A tris-sulfated heparin disaccharide .DELTA.UA2S.alpha.1-4GIcNS6S) showed some inhibition of **L**-**selectin**-Ig binding (FIG. 8). Comparisons of heparin tetrasaccharides to sLe.sup.x in blocking L- and P-selectin Ig binding to BSA-sLe.sup.x are shown. : .

DETDESC:

DETD(30)

By . . . activity at concentrations of up to 1 mM in this assay. sLe.sup.x has been reported to block approximately 50% of

L-**selectin**-Ig binding to immobilized sLe.sup.x glycolipid at a concentration of 5 mM (Foxall, et al., J. Cell. Biol. 117:895, 1992), and approximately 60% of **L**-**selectin**-Ig binding to a high endothelial venule-derived glycoprotein, glycam-1, at 11 mM (Imai, et al., Glycobiology, 2:373, 1992). Thus, the F4 heparin tetrasaccharide appears to be over 100-fold more active than sLe.sup.x against **L**-**selectin** in non-cellular assays. Consistent with previous studies, sLe.sup.x blocked **E**-**selectin**-Ig binding to immobilized BSA-sLe.sup.x with an IC.sub.50 of 510.+-.60 .mu.M; the F4 heparin tetrasaccharide, like the heparin tetrasaccharide mixture, had no activity against **E**-**selectin**-Ig at concentrations up to 1 mM.

US PAT NO: 5,519,008 [IMAGE AVAILABLE] L3: 4 of 23
TITLE: Derivatives of triterpenoid acids as inhibitors of cell-adhesion molecules **ELAM**-1 (**E**-**selectin**) and LECAM-1 (**L**-**selectin**)

SUMMARY:

BSUM(5)

A . . . (hereinafter LEC-CAMs) in many of the initial interactions between leukocytes and vascular endothelia. The three known members of this family, **L**-**Selectin** (LECAM-1, LAM-1, gp90MEL), **E**-**Selectin** (LECAM-2, **ELAM**-1) and P-Selectin (LECAM-3, GMP-140, PADGEM), each contain a domain with homology to the calcium-dependent lectins (C-lectins), an EGF-like domain, and. . .

US PAT NO: 5,508,387 [IMAGE AVAILABLE] L3: 5 of 23

SUMMARY:

BSUM(6)

Adhesion . . . of the inflammatory response. Several receptors have been implicated in this interaction, including a family of putative lectins that includes **L**-**selectin** (gp90.sup.MEL, Leu8), P-selectin (GMP-140, PADGEM) and **E**-**selectin** (**ELAM**-1) (Gong et al., Nature (1990) 343:757; Johnston et al., Cell (1989) 56:1033; Geoffrey et al., J Cell Biol (1989) 109:2463;. . .

US PAT NO: 5,494,790 [IMAGE AVAILABLE] L3: 6 of 23

SUMMARY:

BSUM(13)

Furthermore, . . . upon the difference in the structure of a sugar chain. In addition, it has been found that a ligand of **ELAM**-1 which is inflammatory response-specifically expressed on blood vessel endothelial cell and promotes adhesion to neutrophil is a sugar chain called. . . Science 250, 1130 (1990), Goelz et al.: Trends in Glycoscience and Glycotechnology 4, 14 (1992)]. Further, it is suggested that **L**-**selectin** which is expressed in a part of T lymphocytes and neutrophil and GMP-140 (also called as P-selectin) which is expressed. . . the membrane surface of platelet and blood vessel endothelial cell by inflammatory stimulation participate in inflammatory response as same as **ELAM**-1, and ligands thereof are also sugar chains similar to

Sialyl-Le.sup.X sugar chain which is a ligand of **ELAM**-1 [Rosen et al.: Trends in Glycoscience and Glycotechnology 4, 1 (1992), Larsen et al.: Trends in Glycoscience and Glycotechnology) 4,. . .

SUMMARY:

BSUM(15)

From . . . is expected that Sialyl-Le.sup.X sugar chain or derivatives thereof manifest the excellent anti-inflammatory effects and anti-metastatic effects by binding to **ELAM**-1, **L**-**selectin** or GMP-140.

SUMMARY:

BSUM(16)

Additionally, . . . of cancer could be prevented by inhibiting the expression of glycosyltransferase which controls synthesis of ligand sugar chain recognized by **ELAM**-1, **L**-**selectin** or GMP-140. Antisense RNA/antisense DNA techniques [Tokuhisa: Bioscience and Industry 50, 322 (1992), Murakami: Chemistry 46, 681 (1991)] or Triple. . .

US PAT NO: 5,489,578 [IMAGE AVAILABLE] L3: 7 of 23

SUMMARY:

BSUM(13)

Presently, the best characterized ligands are the HEV-associated ligands for **L**-**selectin**, known as GlyCAM-1 (previously termed Sgp50) and Sgp90 (Imai, Y., Singer, M. S., Fennie, C., Lasky, L. A., and Rosen,. . . oligosaccharide chains and were originally detected by precipitation of lymph node extracts, metabolically labeled with .sup.35 SO.sub.4, with a soluble **L**-**selectin**/immunoglobulin chimera. Other lower affinity ligands may exist that fail to be precipitated by the chimera but nonetheless participate in functionally. . . multiple charges, the major contribution apparently coming from sulfation rather than sialylation. The interaction of both GlyCAM-1 and Sgp90 with **L**-**selectin** depends on their sialylation, confirming earlier findings that sialidase treatment of lymph node HEV impairs lymphocyte attachment and lymphocyte trafficking. . . as a ligand. Furthermore, both in competitive inhibition studies and direct binding studies, sLe.sup.x -type oligosaccharides manifest ligand activity for **L**-**selectin** whereas the Lewis X-type structures with .alpha.2.fwdarw.6 linked Neu5Ac are inactive (Foxall, C., Watson, S. R., Dowbenko, D., Fennie, C.,. . . contribution from fucose is suspected, since sialyllactose (i.e., Neu5Ac.alpha.2.fwdarw.3Gal.beta.1.fwdarw.4Glc) as compared to sLe.sup.x is relatively inactive as a competitor of **L**-**selectin** binding. Moreover, fucose has been shown to be a critical determinant for the neutrophil ligands for P- and **E**-**selectin** (Larsen, G. R., Sako, D., Ahern, T. J., Shaffer, M., Erban, J., Sajer, S. A., Gibson, R. M., Wagner, D.. . . and in light of the sequence similarity among the lectin domains of the selectins is likely to be important for **L**-**selectin** ligands as well.

DETDESC:

DETD(5)

Some standard abbreviations used in connection with the present invention include: BSA, bovine serum albumin; DEAE, diethylaminoethyl; DMSO, dimethylsulfoxide; **ELAM**-1, endothelial/leukocyte adhesion molecule-1 (also **E**-**selectin**); HPTLC, high performance thin layer chromatography; LECAM-1, leukocyte/endothelial cell adhesion molecule-1 (also **L**-**selectin**); MOPS, 3-[N-Morpholino]propanesulfonic acid; NANA, N-acetylneuraminic acid; PVC, polyvinylchloride; TLC, thin layer chromatography; TFA, trifluoroacetic acid; Tris, tris (hydroxymethyl) aminomethane; C-type,. . .

DETDESC:

DETD(15)

Replacement . . . that sialic acid can be replaced by sulfate in sialyl Lewis X with the preservation of ligand activity for both **E**-**selectin** (Yuen, C. T., Lawson, A. M., Chai, W., Larkin, M., Stoll, M. S., Stuart, A. C., Sullivan, F. X., Ahern, T. J. & Feizi, T. Biochemistry (1992) 31:9126-9131) and **L**-**selectin** (Green, P. J., Tamatani, T., Watanabe, T., Miyasaka, M., Hasegawa, A., Kiso, M., Yuen, C. T., Stoll, M. S., &. . .

DETDESC:

DETD(44)

Previous work has demonstrated that **E**-**selectin**, Lowe, J. B., Stoolman, L. M., Nair, R. P., Larsen, R. D., Berhend, T. L. & Marks, R. M., Cell,. . . E., Nudelman, E., Singhal, A. K., Hakomori, S. & Paulson, J. C., Proc. Natl. Acad. Sci. (USA), 88:6224-6228 (1991) and **L**-**selectin** Imai, Y., Lasky, L. A. and Rose, S. D., Glycobiology, 2:373-381 (1992); Foxall et al., J. Cell Biol., 117:895-902 (1992),. . .

US PAT NO: 5,486,536 [IMAGE AVAILABLE] L3: 8 of 23

SUMMARY:

BSUM(7)

Besides . . . sialyl Lewis.sup.x and sialyl Lewis.sup.a) (C-T. Yuen et al., Biochem. 31 9126 (1992)). Most of these lectins are reactive with **L**-**selectin**, while binding to P- and **E**-**selectin** has been variously reported (G. Todderud et al., J. Leukoc. Biol. 52, 85 (1992)). Virtually nothing is known regarding the. . .

DETDESC:

DETD(15)

Precisely . . . selectin(s) is/are being blocked by sulfatide is not clear at present. Sulfatides have been shown to be reactive with rat **L**-**selectin** (Y. Suzuki, et al., Biochem. Biophys. Res. Comm. 190, 426 (1993)), and this is supported by the data in Table. . . possible that infused sulfatide was reactive with either P-selectin (in the case of the CVF model of lung injury) or **E**-**selectin** (in the case of

IgG immune complex-induced lung injury). Sulfoglucuronyl glycosphingolipids have been reported to bind to P- and L-selectins but not to **E**-**selectin** (L. K. Needham et al., Proc. Natl. Acad. Sci. USA 90, 1359 (1993)). The bulk of evidence related to interactions of sulfated compounds with selectins suggests that **E**-**selectin** is less reactive when compared to P- and **L**-**selectin** (G. Todderud et al., J. Leukoc. Biol. 52, 85 (1992)).

US PAT NO: 5,484,891 [IMAGE AVAILABLE] L3: 9 of 23

SUMMARY:

BSUM(13)

The three members of the LEC-CAM or selectin family of cell adhesion molecules are: **L**-**selectin** (a.k.a. peripheral lymph node homing receptor (pnHR), LEC-CAM-1, LAM-1, gp90.sup.MEL, gp100.sup.MEL, gp110.sup.MEL, MEL-14 antigen, Leu-8 antigen, TQ-1 antigen, DREG antigen), **E**-**selectin** (LEC-CAM-2, LECAM-2, **ELAM**-1) and P-selectin (LEC-CAM-3, LECAM-3, GMP-140, PADGEM). These receptors will further on be referred to as "selectins". The structures of the. . .

DRAWING DESC:

DRWD(3)

FIG. 1 illustrates the structures of the selectin (LEC-CAM) family members as determined by cDNA cloning. Illustrated are the structures for **L**-**selectin**, **E**-**selectin** and P-selectin. The lectin, epidermal growth factor (EGF), and multiple short consensus repeats (SCRs) are shown with hypothetical disulfide bond. . .

DRAWING DESC:

DRWD(4)

FIG. . . . structure of the genes encoding members of the selectin family. Illustrated are the genomic structures encoding both human and murine **L**-**selectin**, human **E**-**selectin** and human P-selectin. The dark boxes show exons that encode the various structural motifs, including the start codon for the. . . near a locus encoding a family of proteins that all contain variable numbers of the short SCR exon. The murine **L**-**selectin** is also encoded on murine chromosome 1 in a region syntonic to that found in the human chromosome 1 homologue.

DETDESC:

DETD(64)

A . . . to use carefully selected oligonucleotide sequences to screen cDNA libraries from various tissues, preferably mammalian lymph node high endothelial venules (**L**-**selectin** ligand), or myeloid cells (**E**-**selectin** and P-selectin ligands). Among the preferred mammals are humans and members of the following orders: bovine, ovine, equine, murine, and. . .

US PAT NO: 5,470,843 [IMAGE AVAILABLE] L3: 10 of 23

SUMMARY:

BSUM(204)

Advantageously, . . . which belong to the class of selectins. Most particularly preferred receptors are those expressed in inflammatory disorders, for example Leu-8 (=**L**-**selectin**=gp90.sup.mel =LAM-1=LEC-CAM-1), **ELAM**-1 (=**E**-**selectin**) and GMP-140 (=P-selectin=CD62=PADGEM).

SUMMARY:

BSUM(248)

The genetic construct "**ELAM**-Rg," published by Walz et al., Science 250:1132-1135 (1990), was used to prepare soluble **L**-**selectin**-IgG1 fusion protein. For expression of recombinant selectin, plasmid DNA was transfected into COS-7 cells (ATCC) using DEAE-dextran. See Ausubel, F.. . .

US PAT NO: 5,464,935 [IMAGE AVAILABLE] L3: 11 of 23

SUMMARY:

BSUM(2)

This invention relates to peptides which inhibit binding of selectins such as P-selectin, **E**-**selectin** and **L**-**selectin**.

SUMMARY:

BSUM(7)

Endothelium . . . appearance of other endothelial surface molecules. The slower cytokine-inducible endothelial adhesion for leukocytes is mediated, at least in part by **E**-**selectin** that is synthesized by endothelial cells after exposure to cytokines and then transported to the cell surface, where it binds neutrophils. The isolation, characterization and cloning of **E**-**selectin**, also known as **ELAM**-1, is reviewed by Bevilacqua, et al., in Science 243, 1160-1165 (1989). **L**-**selectin**, also known as peripheral lymph node homing receptor, "the murine Mel 14 antigen" "Leu 8" the "Leu 8 antigen" and. . .

SUMMARY:

BSUM(12)

Peptides . . . discloses that peptide sequences within the lectin domain of P-selectin, having homology with the lectin domains of other proteins, especially **E**-**selectin** and **L**-**selectin**, selectively inhibit neutrophil adhesion to purified P-selectin, and can therefore be used in diagnostic assays of patients and diseases characterized. . .

SUMMARY:

BSUM(13)

P-selectin, **E**-**selectin**, and **L**-**selectin** constitute the selectin family, based on their related structure and function. **E**-**selectin** is not present in unstimulated endothelium. However, when endothelium is exposed to cytokines such as tumor necrosis factor of interleukin-1, the gene for **E**-**selectin** is transcribed, producing RNA which in turn is translated into protein. The result is that **E**-**selectin** is expressed on the surface of endothelial cells one to four hours after exposure to cytokines, as reported by Bevilacqua. . . (1987) (in contrast to P-selectin, which is stored in granules and presented on the cell surface within seconds after activation). **E**-**selectin** has been shown to mediate the adherence of neutrophils to cytokine-treated endothelium and thus appears to be important in allowing leukocytes to migrate across cytokine-stimulated endothelium into tissues. The cDNA-derived primary structure of **E**-**selectin** indicates that it contains a "lectin" domain, an EGF domain, and six (instead of the nine in GMP-140) repeats similar. . . those of complement-regulatory proteins, a transmembrane domain, and a short cytoplasmic tail. There is extensive sequence homology between P-selectin and **E**-**selectin** throughout both proteins, but the similarity is particularly striking in the lectin and EGF domains.

SUMMARY:

BSUM(15)

Based on a comparison of the lectin domains between P- E- and **L**-**selectin**, it may be possible to select those peptides inhibiting binding of neutrophils to P-selectin which will inhibit binding of **E**-**selectin**, **L**-**selectin** and other homologous molecules, to components of the inflammatory process, or, conversely, which will inhibit only one selectin- mediated binding.

SUMMARY:

BSUM(20)

It is therefore an object of the present invention to provide peptides interacting with cells recognized by selectins, including P-selectin, **E**-**selectin**, and **L**-**selectin**.

DETDESC:

DETD(46)

Since the selectins have several functions related to leukocyte adherence, inflammation, and coagulation, compounds which interfere with binding of P-selectin, **E**-**selectin** or **L**-**selectin** can be used to modulate these responses.

US PAT NO: 5,464,815 [IMAGE AVAILABLE] L3: 12 of 23

SUMMARY:

BSUM(5)

It . . . latter see also Liu et al., Am. J. Physiol. 263 (Gastrointest. Liver Physiol. 26): G642-G649 (1992)); and selectins, such as **L**-**selectin**, **E**-**selectin** and P-selectin

(Norgard-Sumnicht et al., Science 261, 480-483 (1993)) .

DETDESC:

DETD(28)

The . . . is used to describe cell adhesion molecules also referred to as LEC-CAMs, the number of which currently stands at three: **L**-**selectin** (a.k.a. periopheral lymphone node homing receptor (pnHR), LEC-CAM-1, LAM-1, gp90.sup.MEL, gp100.sup.MEL, gp110.sup.MEL, MEL-14 antigen, Leu-8 antigen, TQ-1 antigen, DREG antigen); **E**-**selectin** (LEC-CAM-2, LECAM-2, **ELAM**-1) and P-selectin (LEC-CAM-3, LECAM-3, GMP-140, PADGEM) (see Belacqua et al., Science 243, 1160 (1989) and Geng et al., Nature 343,. . .

DETDESC:

DETD(39)

In another preferred embodiment, the heparin binding protein is a selectin or a functional derivative thereof. The selectin preferably is **L**-**selectin** (U.S. Pat. No. 5,098,833 issued 24 Mar. 1992) or **E**-**selectin**. Functional derivatives of selectins are also known are and, for example, disclosed in U.S. application Ser. No. 07/879,036 filed 30. . . substitution at position 8. In particular, the substitution of alanine for glutamic acid (a charged residue) at position 8 of **E**-**selectin**, and the mutation of lysine to alanine at this site in L- and P-selectin was found to significantly enhance ligand. . .

US PAT NO: 5,464,778 [IMAGE AVAILABLE] L3: 13 of 23

SUMMARY:

BSUM(4)

E-**selectin** (**ELAM**-1) is a cytokine-inducible endothelial cell receptor for neutrophils, as reported by Bevilacqua et al., "Identification of an inducible endothelial leukocyte. . . and functional interactions" Proc. Natl. Acad. Sci. USA 87:1673-1677 (1990), and memory T cells, as reported by Picker et al., "**ELAM**-1 is an adhesion molecule for skin homing T cells" Nature (London) 349:796-799 (1991); Shimizu et al., "Activation-independent binding of human memory T cells to adhesion molecule **ELAM** 1" Nature (London) 349:799-802 (1991). **L**-**selectin** (LAM-1, LECAM-1), a protein expressed on myeloid cells and most lymphocytes, participates in neutrophil extravasation into inflammatory sites and homing. . .

DETDESC:

DETD(54)

Based on studies in which an antibody to **L**-**selectin** (DREG-56) partially inhibited neutrophil adhesion to P-selectin-transfected cells, it was suggested that **L**-**selectin** is an important glycoprotein ligand on myeloid cells for P-selectin by Picker et al., "The neutrophil selectin LECAM-1 presents carbohydrate ligands to the vascular selectins **ELAM**-1 and GMP-140" Cell 66:921-933 (1991). Although

L-**selectin** is present in membrane extracts and WGA eluates of neutrophil membranes, as detected by Western blotting, [.sup.125 I]P-selectin did not bind to **L**-**selectin** in the blotting assay. In addition, the anti-**L**-**selectin** mAb DREG-56 (100 .mu.g/ml) had no effect on the binding of purified P-selectin to quiescent neutrophils as assessed by flow cytometry. Neutrophils were preincubated for 15 min with buffer alone, 100 .mu.g/ml of the anti-**L**-**selectin** monoclonal antibody DREG-56, or 100 .mu.g/ml of the anti-P-selectin mAb G1 before addition of buffer or P-selectin. P-selectin binding was. . .

DETDESC:

DETD(84)

Since . . . leukocyte adherence, inflammation, tumor metastases, and coagulation, clinically, compounds which interfere with binding of P-selectin and/or the other selectins, including **E**-**selectin** and **L**-**selectin**, such as the carbohydrates, can be used to modulate these responses. These compounds include the P-selectin ligand, antibodies to the. . .

US PAT NO: 5,460,945 [IMAGE AVAILABLE] L3: 14 of 23

DETDESC:

DETD(24)

The . . . addressin) (Berg et al., 1991, J. Cell Biol. 114: 343) is the homing receptor selectin, also called LAM-1, LECAM-1, or **L**-**selectin**, which is expressed on all leukocytes and facilitates lymphocyte binding to endothelium during blood circulation through peripheral lymph nodes and lymphocyte and neutrophil binding to endothelium at inflammatory sites. The **ELAM**-1 glycoprotein is synthesized by endothelial cells in response to inflammatory agents and promotes adhesion of a variety of leukocytes. The. . .

DETDESC:

DETD(108)

A preferred specific embodiment for testing numerous compounds for inhibitory activity is as follows: As cells are continuously rolling on **E**-**selectin**, P-selectin, or the ligand of **L**-**selectin** in a parallel plate flow chamber of a rolling model apparatus of the invention, a test compound is injected for. . .

US PAT NO: 5,444,050 [IMAGE AVAILABLE] L3: 15 of 23

SUMMARY:

BSUM(4)

E-**selectin**, which has also been called **ELAM**-1 for endothelial leukocyte adhesion molecule-1 and LECAM-2 for lectin cell adhesion molecule, is a glycoprotein that is found on the surface of endothelial cells, the cells that line the interior wall of capillaries. **E**-**selectin** recognizes and binds to the carbohydrate sialyl-Lewis.sup.x (sLe.sup.x), which is present on the surface of

certain white blood cells. **E**-**selectin** helps white blood cells recognize and adhere to the capillary wall in areas where the tissue surrounding the capillary has been infected or damaged. **E**-**selectin** is actually one of three selectins now known. The other two are **L**-**selectin** and P-selectin. P-selectin is expressed on inflamed endothelium and platelets, and has much structural similarity to **E**-**selectin** and can also recognize sialyl-Lewis.sup.x. The structure of sialyl-Lewis.sup.x and sialyl-Lewis.sup.a (sLe.sup.a) are shown in formulas I.sub.a and I.sub.b below:. . .

US PAT NO: 5,440,015 [IMAGE AVAILABLE] L3: 16 of 23

SUMMARY:

BSUM(5)

One . . . autoimmune responses. Several receptors have been implicated in this interaction, including a family of putative lectins that includes gp90.sup.MEL (Leu8), **ELAM**-1, and GMP-140 (PADGEM) and (Gong, J. -G., et al., Nature (1990) 343:757; Johnston, G. I., et al., Cell (1989) 56:1033;. . . S. D., J. Cell Biol. (1989) 109:2463; Lasky, L. A., et al., Cell (1989) 56:1045). These lectins have been termed **L**-**SELECTIN**, **E**-**SELECTIN**, and P-SELECTIN.

SUMMARY:

BSUM(8)

In contrast to **E**-**SELECTIN**, the properties of the ligands that bind to **L**-**SELECTIN** and P-SELECTIN are not as well worked out. **L**-**SELECTIN** appears to bind a sialic acid bearing ligand based on neuraminidase treatment of peripheral lymph node high endothelial venules which inhibits **L**-**SELECTIN** recognition. True et al., 1990, J. Cell Biol. 111, 2757-2764. Further, other studies using soluble **L**-**SELECTIN** in direct binding/inhibition assays suggests that certain carbohydrate moieties may be important ligand components including mannose and fucose, particularly when sulfated or phosphorylated. Imai et al., 1990 J. Cell Biol. 111, 1225-1232. More recent studies suggest that **L**-**Selectin** binds to sialyl Lewis X. Foxall, C., et al., (1992) J. Cell Biology, 117:895-902.

DETDESC:

DETD(15)
The amino acid sequence shown in formula 2 is present in the P-SELECTIN, **E**-**SELECTIN** and **L**-**SELECTIN** lectin domains. The single letter code is used to denote the known amino acids.

DETDESC:

DETD(21)

In their most general form assays for identifying peptides that interfere with selectin ligand binding involve contacting the appropriate selectin, **L**-**SELECTIN**, **E**-**SELECTIN**, or P-SELECTIN, with an appropriate ligand in the presence of peptide, and measuring the degree to which the peptide inhibits. . .

DETDESC:

DETD(22)

Several assays are available to measure the capacity of a peptide to interfere with selectin ligand binding to **L**-**SELECTIN**, **E**-**SELECTIN**, or P-SELECTIN, and such assays are well known in the art. For example, both the selectin and the ligand may. . .

DETDESC:

DETD(25)

A variation of the above assay is to genetically engineer cells to express high levels of **L**-**SELECTIN**, **E**-**SELECTIN**, or P-SELECTIN on their surface, and to use the cells in lieu of purified selectin. Radiolabeled COS cells have been used in this type of assay, and can be transfected with cDNA that encodes for **L**-**SELECTIN**, **E**-**SELECTIN** or P-SELECTIN. After the cells have had a sufficient time to adhere to the ligand coated microtiter well, in the. . . decrease in the number of adherent cells. Representative of the application of this type of assay is the identification of **E**-**SELECTIN** ligands. For example, a complete cDNA for the **ELAM**-1 receptor was obtained by PCR starting with total RNA isolated from IL-1 stimulated human umbilical vein endothelium. The resulting cDNA. . . to generate COS cells that support HL-60 cell adhesion. DNA sequencing positively identified one of these clones as encoding for **ELAM**-1 (Bevilacqua, M. P., et al., Science, (1989) 243:1160; Polte, T., et al., Nucleic Acids Res. (1990) 18:1083; Hession, C., et al., Proc. Natl. Acad. Sci. USA (1990) 87:1673). These publications are incorporated herein by reference for their disclosure of **ELAM**-1 and genetic material coding for its production. The complete nucleotide sequence of the **ELAM**-1 cDNA and predicted amino acid sequence of the **ELAM**-1 protein are given in the above cited article by Bevilacqua et al., which DNA and amino acid sequences are incorporated. . .

DETDESC:

DETD(28)

Similarly, COS cells may be transfected with cDNAs that encode **L**-**SELECTIN** and/or P-SELECTIN. The production and characterization of **L**-**SELECTIN** IgG chimera constructs have been previously described by Watson S. R. et al., (1990) J. Cell Biol. 110:2221-2229. This chimera. . . a suitable host cell, for example, 293 cells and purified. Protein A affinity chromatography is the preferred method of purification. **E**-**SELECTIN** and P-SELECTIN may be constructed with truncated complement binding domains to standardize the size of the chimeras and to facilitate their secretion. A variation of the above assay is to genetically engineer cells to express high levels of **L**-**SELECTIN**, **E**-**SELECTIN**, or P-SELECTIN on their surface, and to use the cells in lieu of purified selectin. Radiolabeled COS cells have been used in this type of assay, and can be transfected with cDNA that encodes for **L**-**SELECTIN**, **E**-**SELECTIN** or P-SELECTIN. After the cells have had a sufficient time to adhere to the ligand coated microtiter well, non-adherent cells. . .

DETDESC:

DETD(45)

It . . . peptides of formulas 1-5 would also have significant therapeutic applications. Such antibody would have the capacity to bind to P-selectin, **E**-**selectin** or **L**-**selectin** and interfere with binding of the selectins to the relevant ligand. This, in turn, would prevent or interfere with cell-cell. . .

US PAT NO: 5,426,113 [IMAGE AVAILABLE] L3: 17 of 23

SUMMARY:

BSUM(5)

Recently, . . . against foreign infections. In the presence of local tissue stimulus such as that caused by a bacteria, adhesion receptors (P-selectin, **E**-**selectin**, intracellular cell adhesion molecule-1 (ICAM-1), etc.) are expressed locally on the walls of the blood vessels. These receptors interact with counter-receptors (**L**-**selectin**, macrophage receptor-1 (MAC-1), etc.) on the neutrophils allowing these cells to slow down via a rolling motion, stop and transmigrate. . .

US PAT NO: 5,418,147 [IMAGE AVAILABLE] L3: 18 of 23

DETDESC:

DETD(11)

Any . . . members of the families of immunoglobulin and cytokine receptors, integrins, and selectins. Specific proteins include CD11A, CD11B, CD4, P- and **L**-**selectin**, **ELAM**-1, FcERI.alpha., IL-1 receptor and p70 of the IL-2 receptor. T-cell receptors, including .alpha., .beta., .gamma., or, .delta. subunits, and MHC. . .

US PAT NO: 5,412,123 [IMAGE AVAILABLE] L3: 19 of 23

DRAWING DESC:

DRWD(9)

FIGS. . . . are respectively graphs showing the ability of a multivalent derivative of sennoside A to inhibit the binding of SLE.sup.x to **E**-**selectin**, **L**-**selectin** and P-selectin.

DETDESC:

DETD(4)

Some standard abbreviations used in connection with the present invention include: BSA, bovine serum albumin; DEAE, diethylaminoethyl; DMSO, dimethylsulfoxide; **ELAM**-1, or **E**-**selectin** endothelial/leukocyte adhesion molecule-1; HPTLC, high performance thin layer chroma-tography; LECAM-1, or **L**-**selectin** leukocyte/endothelial cell adhesion molecule-1; MOPS, 3-[N-Morpholino]propanesulfonic acid; NANA, N-acetylneuraminic acid; PVC, polyvinylchloride; TLC, thin layer chromatography; TFA, trifluoroacetic

acid; Tris,. . .

DETDESC:

DETD(110)

The . . . plates were washed with H.sub.2 O and blocked with 5% BSA in PBS with 1 mM Ca for 1 hour. **L**-**selectin** was diluted to 35 ng/ml in 1% BSA PBS with 1 mM Ca and 1:1500 biotinylated goat F(ab') anti-human IgG Fc (CalTag, corp.) and streptavidin-alkaline phosphatase. **E**-**selectin** at 50 ng/ml and P-selectin at 750 ng/ml were similarly diluted with 1:1000 dilutions of biotinylated goat F(ab') anti-human IgG. . .

US PAT NO: 5,389,520 [IMAGE AVAILABLE] L3: 20 of 23

SUMMARY:

BSUM(6)

Several . . . One of the several molecules involved in the initial attachment of leukocytes to endothelium is the leukocyte adhesion molecule-1 (LAM-1, **L**-**selectin**) (Kishimoto et al., Proc. Natl. Acad. Sci. USA 87:2244-2248 (1990); Ley et al., Blood 77:2553-2555 (1991); Spertini et al., J.. . . al., Proc. Natl. Acad. Sci. USA 86:5562-5566 (1989); Tedder et al., J. Exp. Med. 170:123-133 (1989)) that includes, the mouse **L**-**selectin**, MEL-14 (Gallatin et al., Nature 304:30-34 (1983); Lasky et al., Cell 56:1045-1055 (1989); Siegelman et al., Science 243:1165-1172 (1989)), Endothelial-Leukocyte Adhesion Molecule-1 (**ELAM**-1, **E**-**selectin**) (Bevilacqua et al., Proc. Natl. Acad. Sci. USA 84:9238-9243 (1987); Bevilacqua et al., Science 243:1160-1164 (1989); Luscinskas et al., J.. . .

US PAT NO: 5,384,249 [IMAGE AVAILABLE] L3: 21 of 23

SUMMARY:

BSUM(16)

Further, it is suggested that **L**-**selectin**, which is expressed in a part of T lymphocytes and neutrophils, and GMP-140 (also called P-selectin), which is expressed in the membrane surface of platelets and blood vessel endothelial cells participate in inflammatory response in the same manner as **ELAM**-1, and ligands thereof are also sugar chains similar to the Sialyl-Le.sup.x sugar chain which is a ligand of **ELAM**-1 [Rosen et al.: Trends in Glycoscience and Glycotechnology 4, 1 (1992), Larsen et al.: Trends in Glycoscience and Glycotechnology 4,. . .

SUMMARY:

BSUM(18)

From . . . expected that the Sialyl-Le.sup.x sugar chain or derivatives thereof may manifest excellent anti-inflammatory effects and anti-metastatic effects by binding to **ELAM**-1, **L**-**selectin** or GMP-140.

SUMMARY:

BSUM(19)

Additionally, . . . be prevented by inhibiting the expression of the glycosyltransferase which controls the synthesis of the ligand sugar chain recognized by **ELAM**-1, **L**-**selectin** or GMP-140. Antisense RNA/antisense DNA techniques [Tokuhisa: Bioscience and Industry 50, 322 (1992), Murakami: Chemistry 46, 681 (1991)] or Triple. . .

US PAT NO: 5,360,733 [IMAGE AVAILABLE] L3: 22 of 23

SUMMARY:

BSUM(11)

In . . . tumor cells often express a significant amount of sialyl Le.sup.x and/or sialyl Le.sup.a on their cell surfaces. The interaction between **E**-**selectin** or P-selectin and these cell surface carbohydrates may play a role in tumor cell adhesion to endothelium during the metastatic. . . cells was abolished by blocking O-glycan synthesis. Complex sulfated O-glycans also may serve as ligands for the lymphocyte homing receptor, **L**-**selectin** (Imai et al., J. Cell Biol. 113:1213-1221 (1991)).

US PAT NO: 5,304,640 [IMAGE AVAILABLE] L3: 23 of 23

SUMMARY:

BSUM(13)

The three members of the LEC-CAM or selectin family of cell adhesion molecules are: **L**-**selectin** (a.k.a. peripheral lymph node homing receptor (pnHR), LEC-CAM-1, LAM-1, gp90.sup.MEL, gp100.sup.MEL, gp110.sup.MEL, MEL-14 antigen, Leu-8 antigen, TQ-1 antigen, DREG antigen), **E**-**selectin** (LEC-CAM-2, LECAM-2, **ELAM**-1) and P-selectin (LEC-CAM-3, LECAM-3, GMP-140, PADGEM). These receptors will selectin family members and of the genes encoding them are illustrated. . .

DRAWING DESC:

DRWD(2)

FIG. 1 illustrates the structures of the selectin (LEC-CAM) family members as determined by cDNA cloning. Illustrated are the structures for **L**-**selectin**, **E**-**selectin** and P-selectin. The lectin, epidermal growth factor (EGF), and multiple short consensus repeats (SCRs) are shown with hypothetical disulfide bond. . .

DRAWING DESC:

DRWD(3)

FIG. . . . structure of the genes encoding members of the selectin family. Illustrated are the genomic structures encoding both human and murine **L**-**selectin**, human **E**-**selectin** and human P-selectin. The dark boxes show exons that encode the various structural motifs,

including the start codon for the. . . near a locus encoding a family of proteins that all contain variable numbers of the short SCR exon. The murine **L**-**selectin** is also encoded on murine chromosome 1 in a region syntonic to that found in the human chromosome 1 homologue.

DETDESC:

DETD(64)

A . . . to use carefully selected oligonucleotide sequences to screen cDNA libraries from various tissues, preferably mammalian lymph node high endothelial venules (**L**-**selectin** ligand), or myeloid cells (**E**-**selectin** and P-selectin ligands). Among the preferred mammals are humans and members of the following orders: bovine, ovine, equine, murine, and. . .
=> d l3 1-23 date

L3: 1 of 23

TITLE: Pretargeting methods and compounds
US PAT NO: 5,541,287 DATE ISSUED: Jul. 30, 1996
[IMAGE AVAILABLE]
APPL-NO: 08/345,811 DATE FILED: Nov. 22, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 156,565, Nov. 22, 1993, abandoned, which is a continuation-in-part of Ser. No. 995,381, Dec. 23, 1992, abandoned, which is a continuation-in-part of Ser. No. 895,588, Jun. 9, 1992, Pat. No. 5,283,342, Feb. 1, 1994.

L3: 2 of 23

TITLE: Derivatives of triterpenoid acids and uses thereof
US PAT NO: 5,527,890 DATE ISSUED: Jun. 18, 1996
[IMAGE AVAILABLE]
APPL-NO: 08/049,018 DATE FILED: Apr. 16, 1993

L3: 3 of 23

TITLE: Selectin receptor modulating compositions
US PAT NO: 5,527,785 DATE ISSUED: Jun. 18, 1996
[IMAGE AVAILABLE]
APPL-NO: 08/089,076 DATE FILED: Jul. 7, 1993
REL-US-DATA: Continuation-in-part of Ser. No. 62,957, May 14, 1993, abandoned.

L3: 4 of 23

TITLE: Derivatives of triterpenoid acids as inhibitors of cell-adhesion molecules **ELAM**-1 (**E**-**selectin**) and LECAM-1 (**L**-**selectin**)
US PAT NO: 5,519,008 DATE ISSUED: May 21, 1996
[IMAGE AVAILABLE]
APPL-NO: 07/943,356 DATE FILED: Sep. 10, 1992

L3: 5 of 23

TITLE: Selectin binding glycopeptides
US PAT NO: 5,508,387 DATE ISSUED: Apr. 16, 1996
[IMAGE AVAILABLE]
APPL-NO: 08/102,032 DATE FILED: Aug. 4, 1993

L3: 6 of 23

TITLE: .alpha.-3 sialyltransferase

US PAT NO: 5,494,790 DATE ISSUED: Feb. 27, 1996
[IMAGE AVAILABLE]
APPL-NO: 08/309,985 DATE FILED: Sep. 20, 1994
FRN-PR. NO: 3-333661 FRN FILED: Dec. 17, 1991
FRN-PR. CO: Japan
FRN-PR. NO: 4-091044 FRN FILED: Apr. 10, 1992
FRN-PR. CO: Japan
REL-US-DATA: Division of Ser. No. 991,587, Dec. 16, 1992, Pat. No. 5,384,249.

L3: 7 of 23

TITLE: Sulfated ligands for l-selectin and methods of treating inflammation
US PAT NO: 5,489,578 DATE ISSUED: Feb. 6, 1996
[IMAGE AVAILABLE]
APPL-NO: 08/432,849 DATE FILED: May 2, 1996
REL-US-DATA: Continuation of Ser. No. 155,947, Nov. 19, 1993, abandoned.

L3: 8 of 23

TITLE: Sulfatides as anti-inflammatory compounds
US PAT NO: 5,486,536 DATE ISSUED: Jan. 23, 1996
[IMAGE AVAILABLE]
APPL-NO: 08/289,585 DATE FILED: Aug. 15, 1994

L3: 9 of 23

TITLE: Selectin ligands
US PAT NO: 5,484,891 DATE ISSUED: Jan. 16, 1996
[IMAGE AVAILABLE]
APPL-NO: 08/018,994 DATE FILED: Feb. 18, 1993
REL-US-DATA: Division of Ser. No. 834,902, Feb. 13, 1992, Pat. No. 5,304,640, which is a continuation-in-part of Ser. No. 695,805, May 6, 1991, Pat. No. 5,318,890.

L3: 10 of 23

TITLE: Carbohydrate-containing polymers, their preparation and use
US PAT NO: 5,470,843 DATE ISSUED: Nov. 28, 1995
[IMAGE AVAILABLE]
APPL-NO: 08/165,805 DATE FILED: Dec. 13, 1993
FRN-PR. NO: 42 41 829.1 FRN FILED: Dec. 11, 1992
FRN-PR. CO: Federal Republic of Germany
FRN-PR. NO: 43 26 777.7 FRN FILED: Aug. 10, 1993
FRN-PR. CO: Federal Republic of Germany

L3: 11 of 23

TITLE: Peptide inhibitors of selectin binding
US PAT NO: 5,464,935 DATE ISSUED: Nov. 7, 1995
[IMAGE AVAILABLE]
APPL-NO: 08/384,680 DATE FILED: Feb. 6, 1995
REL-US-DATA: Continuation of Ser. No. 891,986, May 28, 1992, abandoned.

L3: 12 of 23

TITLE: Inhibition of heparin-binding
US PAT NO: 5,464,815 DATE ISSUED: Nov. 7, 1995
[IMAGE AVAILABLE]
APPL-NO: 08/254,390 DATE FILED: Jun. 6, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 118,162, Sep. 8, 1993,

abandoned.

L3: 13 of 23

TITLE: Glycoprotein ligand for P-selectin and methods of use thereof

US PAT NO: 5,464,778 DATE ISSUED: Nov. 7, 1995
[IMAGE AVAILABLE]

APPL-NO: 08/278,551 DATE FILED: Jul. 21, 1994

REL-US-DATA: Continuation of Ser. No. 976,552, Nov. 16, 1992, abandoned, which is a continuation-in-part of Ser. No. 650,484, Feb. 5, 1991, abandoned, which is a continuation-in-part of Ser. No. 554,199, Jul. 17, 1990, abandoned, which is a continuation-in-part of Ser. No. 320,408, Mar. 8, 1989, Pat. No. 5,378,464.

L3: 14 of 23

TITLE: Device and method for analysis of blood components and identifying inhibitors and promoters of the inflammatory response

US PAT NO: 5,460,945 DATE ISSUED: Oct. 24, 1995
[IMAGE AVAILABLE]

APPL-NO: 07/887,444 DATE FILED: May 20, 1992

REL-US-DATA: Continuation-in-part of Ser. No. 707,841, May 30, 1991, abandoned.

L3: 15 of 23

TITLE: Binding of E-selectin or P-selectin to sialyl Lewis.sup.x or sialyl-Lewis.sup.a

US PAT NO: 5,444,050 DATE ISSUED: Aug. 22, 1995
[IMAGE AVAILABLE]

APPL-NO: 08/235,293 DATE FILED: Apr. 29, 1994

L3: 16 of 23

TITLE: Selectin peptide medicaments for treating disease

US PAT NO: 5,440,015 DATE ISSUED: Aug. 8, 1995
[IMAGE AVAILABLE]

APPL-NO: 08/038,385 DATE FILED: Mar. 29, 1993

REL-US-DATA: Continuation-in-part of Ser. No. 917,487, Jul. 21, 1992, abandoned.

L3: 17 of 23

TITLE: Method of preventing ulcer formation caused by nonsteroidal antiinflammatory drugs employing tetrazol-benzothiophene carboxamide compounds

US PAT NO: 5,426,113 DATE ISSUED: Jun. 20, 1995
[IMAGE AVAILABLE]

APPL-NO: 08/224,891 DATE FILED: Apr. 8, 1994

L3: 18 of 23

TITLE: Glycosyl-phosphatidylinositol-specific phospholipase D

US PAT NO: 5,418,147 DATE ISSUED: May 23, 1995
[IMAGE AVAILABLE]

APPL-NO: 07/860,825 DATE FILED: Mar. 31, 1992

REL-US-DATA: Continuation-in-part of Ser. No. 588,896, Sep. 27, 1990, abandoned.

L3: 19 of 23

TITLE: Anthraquinone and anthracene derivatives as inhibitors of

the cell-adhesion molecules of the immune system

US PAT NO: 5,412,123 [IMAGE AVAILABLE] DATE ISSUED: May 2, 1995
APPL-NO: 08/014,913 DATE FILED: Feb. 8, 1993

L3: 20 of 23

TITLE: Specific detection of cell surface receptor leukocyte adhesion molecule-1
US PAT NO: 5,389,520 [IMAGE AVAILABLE] DATE ISSUED: Feb. 14, 1995
APPL-NO: 07/862,483 DATE FILED: Apr. 2, 1992
REL-US-DATA: Continuation-in-part of Ser. No. 730,503, Jul. 8, 1991, abandoned, which is a continuation of Ser. No. 313,109, Feb. 21, 1989, abandoned, and a continuation-in-part of Ser. No. 700,773, May 15, 1991, abandoned, and a continuation-in-part of Ser. No. 737,092, Jul. 29, 1991, abandoned, and a continuation-in-part of Ser. No. 770,608, Oct. 3, 1991.

L3: 21 of 23

TITLE: .alpha.2.fwdarw.3 sialyltransferase
US PAT NO: 5,384,249 [IMAGE AVAILABLE] DATE ISSUED: Jan. 24, 1995
APPL-NO: 07/991,587 DATE FILED: Dec. 16, 1992
FRN-PR. NO: 3-333661 FRN FILED: Dec. 17, 1991
FRN-PR. CO: Japan
FRN-PR. NO: 4-091044 FRN FILED: Apr. 10, 1992
FRN-PR. CO: Japan

L3: 22 of 23

TITLE: Human .beta.1-6 n-acetylglucosaminyl transferase
US PAT NO: 5,360,733 [IMAGE AVAILABLE] DATE ISSUED: Nov. 1, 1994
APPL-NO: 07/955,041 DATE FILED: Oct. 1, 1992

L3: 23 of 23

TITLE: DNA sequence encoding a selectin ligand
US PAT NO: 5,304,640 [IMAGE AVAILABLE] DATE ISSUED: Apr. 19, 1994
APPL-NO: 07/834,902 DATE FILED: Feb. 13, 1992
REL-US-DATA: Continuation-in-part of Ser. No. 695,805, May 6, 1991.
=>

```
=> e jutila/in
E#      FILE              FREQUENCY  TERM
--      ----              ---------  ----
E1      USPAT                     1      JUTERBOCK, KARSTEN/IN
E2      USPAT                     1      JUTIER, PIERRE/IN
E3      USPAT                     0 --> JUTILA/IN
E4      USPAT                     1      JUTILA, PENTTI K/IN
E5      USPAT                     1      JUTILA, RAYMOND E/IN
E6      USPAT                     2      JUTILA, RAYMOND EINO/IN
E7      USPAT                     1      JUTKEVICH, VALERY I/IN
E8      USPAT                     1      JUTKEVICH, VALERY IVANOVICH/IN
E9      USPAT                     1      JUTO, JAN ERIK/IN
E10     USPAT                     1      JUTO, YASURO/IN
E11     USPAT                     1      JUTRAS, GILLES/IN
E12     USPAT                     1      JUTRAS, GUY F/IN
=> s e1(w)246
         10731 EL
         50205 246
L2           1 EL(W)246
=> d l2 1

1.  5,389,671, Feb. 14, 1995, 4- or 5-(substituted sulfonyl)methyl-3(2H)-
furanones; Steven W. Felman, et al., 514/473 [IMAGE AVAILABLE]
=> d l2 1 kwic

US PAT NO:     5,389,671 [IMAGE AVAILABLE]                L2: 1 of 1

DETDESC:

DETD(65)

 Prepared . . . C.; .sup.1 H NMR (CDCl.sub.3, 400 MHz): .delta.1.39
(s, 6H), 1.40 (s, 9H), 3.83 (s, 2H), 8.44 (s, 1H); MS (**El**): **246**
(M.sup.+), 127 (100); Analysis calc'd for C.sub.11 H.sub.14 O.sub.4 S: C,
53.64; H, 7.36%; Found: C, 43.51; H, 4.59%.
=> s e(w)selectin and l(w)selectin and common(p)epitope?
       1255890 E
           144 SELECTIN
            82 E(W)SELECTIN
        490329 L
           144 SELECTIN
            51 L(W)SELECTIN
        572196 COMMON
          3557 EPITOPE?
           493 COMMON(P)EPITOPE?
L3           3 E(W)SELECTIN AND L(W)SELECTIN AND COMMON(P)EPITOPE?
=> d l3 1-3

1.  5,622,701, Apr. 22, 1997, Cross-reacting monoclonal antibodies
specific for E- and P-selectin; Ellen L. Berg, 424/153.1, 143.1, 152.1,
172.1, 173.1; 435/70.21, 172.2, 334, 343; 530/387.1, 387.3, 388.1,
388.22, 388.7, 389.6; 536/23.53 [IMAGE AVAILABLE]

2.  5,593,882, Jan. 14, 1997, Selectin variants; David V. Erbe, et al.,
435/358, 69.1, 172.3, 252.3, 252.33, 320.1, 325, 369; 514/8; 530/395;
536/23.1, 23.5; 935/10 [IMAGE AVAILABLE]

3.  5,464,815, Nov. 7, 1995, Inhibition of heparin-binding; Steven
```

Chamow, et al., 514/8; 424/85.2; 436/86, 87; 514/21; 530/412 [IMAGE AVAILABLE]
=> d l3 1-3 date

L3: 1 of 3

TITLE: Cross-reacting monoclonal antibodies specific for E- and P-selectin
US PAT NO: 5,622,701 [IMAGE AVAILABLE] DATE ISSUED: Apr. 22, 1997
APPL-NO: 08/259,963 DATE FILED: Jun. 14, 1994

L3: 2 of 3

TITLE: Selectin variants
US PAT NO: 5,593,882 [IMAGE AVAILABLE] DATE ISSUED: Jan. 14, 1997
APPL-NO: 08/274,661 DATE FILED: Jul. 13, 1994
REL-US-DATA: Continuation of Ser. No. 956,701, Oct. 1, 1992, abandoned, which is a continuation-in-part of Ser. No. 879,036, Apr. 30, 1992, abandoned.

L3: 3 of 3

TITLE: Inhibition of heparin-binding
US PAT NO: 5,464,815 [IMAGE AVAILABLE] DATE ISSUED: Nov. 7, 1995
APPL-NO: 08/254,390 DATE FILED: Jun. 6, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 118,162, Sep. 8, 1993, abandoned.
=> d l3 1-3 kwic

US PAT NO: 5,622,701 [IMAGE AVAILABLE] L3: 1 of 3

ABSTRACT:
The invention provides monoclonal antibodies that specifically bind to P-selectin and to **E**-**selectin**. Many of the antibodies block the functional interactions of P-selectin and **E**-**selectin** with the irrespective counterreceptors.

DETD(19)

The . . . to both P- and E-selectins. That is, a single binding site on an antibody has affinity for both P- and **E**-**selectin**. Thus, the antibodies bind to **epitopes** that are **common** to both molecules. The antibodies bind to the natural and/or recombinant human forms for P- and **E**-**selectin** (see Johnston et al., 1989, supra; Bevilacqua et al., 1989 supra). Some antibodies may also bind P- and/or **E**-**selectin** from non human species. Some of the antibodies also specifically bind to **L**-**selectin** (preferably human **L**-**selectin** (see Tedder, EPA386, 906 (1990))whereas other antibodies of the invention do not. Surprisingly, the **common** **epitopes** bound by the crossreacting antibodies of the invention are also **epitopes** important for both E- and P-selectin to interact with their counterreceptors on activated leukocytes, such as neutrophils. Thus, most crossreacting antibodies of the invention block the functional interactions of **E**-**selectin** or P-selectin and usually those of both of these molecules. Some crossreacting antibodies also block the functional interactions of **L**-**selectin** whereas others do not.

SUMMARY:

BSUM(6)

There are three members identified so far in the selectin family of cell adhesion molecules: **L**-**Selectin** (a.k.a. peripheral lymph node homing receptor (pnHR), LEC-CAM-1, LAM-1, gp.sup.90.spsp.MEL, gp.sup.100.spsp.MEL, gp.sup.110.spsp.MEL, MEL-14 antigen, Leu-8 antigen, TQ-1 antigen, DREG antigen), **E**-**Selectin** (LEC-CAM-2, LECAM-2, ELAM-1) and P-Selectin (LEC-CAM-3, LECAM-3, GMP-140, PADGEM). The structures of the selectin family members are illustrated in FIG.. . .

SUMMARY:

BSUM(7)

L-**Selectin** is found on leukocytes and is involved with the trafficking of lymphocytes to peripheral lymphoid tissues [Gallatin et al., Nature. . . 30-34 (1983)] and with acute neutrophil-mediated inflammatory responses [Watson, S. R., Nature 349 164-167 (1991)]. The amino acid sequence of **L**-**Selectin** and the encoding nucleic acid sequence are, for example, disclosed in U.S. Pat. No. 5,098,833 issued 24 Mar. 1992. **L**-**Selectin** appears to recognize sialylated, fucosylated, sulfated carbohydrate ligand(s) on at least two endothelial glycoproteins [True, D. D., et al., J.. . .

SUMMARY:

The model of **E**-**Selectin** was generated based on the crystal structure of the rat mannose-binding protein (MBP) [Weis et al., 1991, Supra). The sequence of **E**-**Selectin** was aligned with those of mouse **L**-**Selectin** (LHR) [Lasky et al., Cell 56, 1045-1055 (1989)] and MBP using the alignment of the latter two proteins provided [Weis et al., 1991, Supra). Eleven insertions and two deletions in **E**-**Selectin** relative to MBP mapped to four surface loops in the MBP structure. MBP (molecule 1) was transformed into **E**-**Selectin** in three steps. First, all residues except those involving insertions/deletions were changed to the **E**-**Selectin** sequence using the INSIGHT-II program (Biosym Technologies, San Diego). If possible, conformations of **E**-**Selectin** side chains were kept similar to those of MBP, otherwise they were based on rotamer libraries [Ponder and Richards, J. Mol. Biol. 193, 775-791 (1987)], packing and hydrogen-bonding considerations. Second, possible loop structures for the **E**-**Selectin** insertions/deletions were gleaned from a search of crystal structures in the Protein Data Bank [Berstein et al., J. Mol. Biol.. . . Third, each of the thirty water molecules present in the MBP crystal structure was evaluated regarding its retention in the **E**-**Selectin** model. Only seven waters were included in the **E**-**Selectin** model, four of which corresponded to MBP water molecules 23, 24, 25 and 30.

DETDESC:

DETD(136)

To facilitate the study of **E**-**Selectin** structure and function, we generated a panel of blocking and non-blocking Mabs directed against human and rabbit **E**-**Selectin** (see Experimental Procedures). Three anti-human **E**-**Selectin** Mabs (7H5, 8E4, and 3B7) were found to inhibit the adhesion of HL60 cells to cytokine activated HUVECs and **E**-**Selectin** transfected COS cells (FIG. 1A). Cross reactivity studies demonstrated that these three blocking Mabs did not recognize rabbit **E**-**Selectin** (FIG. 1B), a result that facilitated the mapping of the epitopes recognized by these Mabs (see below). The commercially available anti-human **E**-**Selectin** MAbs, BBA1, BBA2 and ENA-1, also did not cross react with rabbit **E**-**Selectin** (FIG. 1B). While none of these three commercial MAb's significantly blocked **E**-**Selectin**-mediated HL60 adherence in our cell adhesion assay (FIG. 1A), BBA2 has clear adhesion blocking activity in cell adhesion assays done. . . activated HUVECs [Leeuwenberg et al., Clin. exp. Immunol. 81 496-500 (1990)]. Furthermore, BBA2 and ENA-1 both effectively inhibit binding of **E**-**Selectin** to immobilized sLex glycolipid (Foxall et al., 1992, Supra). Since sLex is the major carbohydrate ligand for **E**-**Selectin** on the leukocyte cell surface, it seemed likely that analysis of the epitopes recognized by this panel of blocking antibodies (7H5, 8E4, 3B7, BBA2 and ENA-1) would indicate the region(s) of **E**-**Selectin** involved with carbohydrate recognition and resultant cell adhesion. In addition, the mapping of regions recognized by other, non-blocking Mabs should. . . the lectin domain not involved with carbohydrate recognition and cell adhesion. Therefore, the initial step in analyzing the regions of **E**-**Selectin** involved in carbohydrate interactions consisted of mapping the epitopes recognized by blocking and non-blocking anti-**E** **Selectin** Mabs.

DETDESC:

DETD(137)
Analysis of **E**-**Selectin** Monoclonal Antibody Binding

DETDESC:

DETD(138)

The **E**-**Selectin** mutagenesis strategy was driven by two major considerations. The first consideration derived from previous work on the localization of the epitope recognized by the murine **L**-**Selectin** blocking Mab, Mel 14 [Bowen et al., J. Cell Biol. 107, 1853-1862 (1990)]. This work demonstrated that this antibody recognized a region within the N-terminal 53 amino acids of murine **L**-**Selectin**. It was assumed that blocking antibodies directed against **E**-**Selectin** may also recognize epitopes contained within the N-terminus of the lectin domain, and this region was, therefore, targeted for mutagenesis.. . .

DETDESC:

DETD(139)

As described above, none of the anti-human **E**-**Selectin** blocking Mabs reacted with rabbit **E**-**Selectin**, and analysis of the amino

acid sequences of the lectin domains of human and rabbit **E**-**Selectin** showed that 5 of 16 differences were clustered in the N terminal nine amino acids (FIG. 2A). To determine whether blocking MAbs map to this region, a chimeric protein containing rabbit **E**-**Selectin** lectin and egf-like domains with the N-terminal 9 amino acids replaced by the corresponding sequence from human **E**-**Selectin** was generated (Hu-Ra-1) (see FIG. 2B). This construct was produced as a fusion of the lectin and egf-like domains with. . . transfected with human lectin-egf-CD16, rabbit lectin-egf-CD16, or the human-rabbit chimera (Hu-Ra-1) demonstrated that human amino acids 1-9 in the rabbit **E**-**Selectin** background were sufficient to confer MAb 7H5 and 8E4 binding but not MAb3B7 binding (FIG. 3). In similar experiments, ENA-1,. . . of the epitopes recognized by three blocking Mabs (7H5, 8E4 and ENA-1) to the N-terminal 9 amino acids of human **E**-**Selectin**.

DETDESC:

DETD(140)

To . . . mapping analysis and allow for direct carbohydrate binding studies (see below), mutations were introduced into the lectin domain of an **E**-**Selectin**-human immunoglobulin G (IgG) chimera that is similar to a previously described **L**-**Selectin**-IgG chimera (FIG. 2B) [Watson et al., 1990, 1991, Supra; Foxall et al., 1992, Supra). The **E**-**Selectin**-IgG chimera allowed for easy quantitation of each individual mutant by analysis of the amount of human IgG produced from each. . . inclusion of the human IgG tail also allowed for rapid analysis of the ability of each mutant to bind the anti-**E**-**Selectin** antibody panel, as well as to immobilized sLex, by use of labeled anti-IgG antibody. In this way, mutants that affected. . .

DETDESC:

DETD(191)

At . . . between E- and P-Selectin must be due to differences in their lectin domains. Transferring the P-Selectin lectin domain onto the **E**-**Selectin**-IgG construct resulted in a molecule (PE-1) which stained cells, albeit at a lower intensity than P-Selectin-IgG. Carbohydrate reactivity was completely. . . domain. Thus, PE-1 reacted with the purified glycolipids in a manner that was indistinguishable from P-Selectin-IgG and quite distinct from **E**-**Selectin**-IgG. Therefore, the lectin domain of each selectin appears sufficient for determining the differences in reactivities with these relatively small sugars.. . . 114: 351-358 (1991)) in which domains of L- and P-Selectin were exchanged to show that PPME and fucoidin binding, both **L**-**Selectin**-specific carbohydrate ligands, as well as the **epitope** defined by blocking mAb LAM1-3, map at least in part to the C-terminal 67 amino acid residues of the **L**-**Selectin** lectin domain. These authors also demonstrated that the CR domains are not important for conferring PPME or fucoidin specificity (Kansas,. . . domain of P-Selectin. The difference in staining between PE-1 and P-Selectin-IgG might reflect subtle conformational effects of the P- or **E**-**Selectin** EGF domains interacting with the **common** lectin domain. However, it is important to stress that protein/protein contacts mediated by the EGF or CR1 domains cannot be. . .

US PAT NO: 5,464,815 [IMAGE AVAILABLE] L3: 3 of 3

SUMMARY:

BSUM(5)

It . . . latter see also Liu et al., Am. J. Physiol. 263 (Gastrointest. Liver Physiol. 26): G642-G649 (1992)); and selectins, such as **L**-**selectin**, **E**-**selectin** and P-selectin (Norgard-Sumnicht et al., Science 261, 480-483 (1993)) .

DETDESC:

US PAT NO: 5,464,815 [IMAGE AVAILABLE] L3: 3 of 3

SUMMARY:

BSUM(5)

It . . . latter see also Liu et al., Am. J. Physiol. 263 (Gastrointest. Liver Physiol. 26): G642-G649 (1992)); and selectins, such as **L**-**selectin**, **E**-**selectin** and P-selectin (Norgard-Sumnicht et al., Science 261, 480-483 (1993)) .

DETDESC:

DETD(15)

"Biological activity" is defined as either 1) immunological cross-reactivity with at least one **epitope** of a native heparin-binding protein, or 2) the possession of at least one adhesive, regulatory or effector function qualitatively in **common** with a native heparin-binding protein.

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      ---  -----  -----------
?begin 55,72,154,399

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            $0.12    0.004 Hrs File1
     $0.12  Estimated cost File1
     $0.12  Estimated cost this search
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SYSTEM:OS  - DIALOG OneSearch
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*File  72: Truncate EMTREE codes(e.g. DC=C1.120?) for complete retrieval.
 Enter HELP RATES 72 for price change.
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*File 399: Use is subject to the terms of your user/customer agreement.

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           21844  EL
            4791  246
              10  EL(W)246
           20127  SELECTIN?
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?rd s1

...completed examining records
      S2       4  RD S1 (unique items)
?t s2/7/all


 2/7/1     (Item 1 from file: 55)
DIALOG(R)File  55:BIOSIS PREVIEWS(R)
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11128707     BIOSIS Number: 97328707
  In vivo and in vitro functional examination of a conserved epitope of L-
and E-selectin crucial for leukocyte-endothelial cell interactions
  Bargatze R F; Kurk S; Watts G; Kishimoto T K; Speer C A; Jutila M A
  Veterinary Mol. Biol. Lab., Montana State University, Bozeman, MT 59717,
USA
  Journal of Immunology 152 (12). 1994.  5814-5825.
  Full Journal Title:  Journal of Immunology
  ISSN: 0022-1767
  Language: ENGLISH
  Print Number: Biological Abstracts Vol. 098 Iss. 003 Ref. 035219
  Selectins  constitute  a three-member gene family of carbohydrate-binding
adhesion  proteins found on the surface of leukocytes and endothelial cells
that  is  central  to  inflammation-associated  leukocyte  recruitment  and
lymphocyte  recirculation. E- and P-selectin are inducible and expressed on
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the surface of endothelial cells under inflammatory conditions, whereas L-selectin is constitutively expressed on most circulating leukocytes. Previously, we have characterized a unique mAb (EL-246) that recognizes a common epitope on both E- and L-selectin, which is presented or determined by their short consensus repeat domains. This report defines the functional properties of EL-246 and its cognate epitope. In a novel in vitro physiologic shear- system, we show that neutrophil rolling on activated HUVECs and on E-selectin cDNA transfectants is blocked 45 to 120 s after infusion of EL-246. The examination of the binding of neutrophils to E-selectin cDNA transfectants reveals that their adhesion is blocked by EL-246 treatment of either cell type. A unique Ab transfer mechanism is demonstrated in which EL-246 is delivered unidirectionally from L- to E-selectin to surpass the adhesion)locked by mAbs that recognize either L- or E-selectin alone. By using flow cytometry and in vivo homing techniques, we show that pretreating bovine lymphocytes with EL-246 blocks their ability to home to mouse peripheral lymph nodes by gt 65%. Cumulatively, these results suggest that EL-246 is a uniquely potent pharmacologic inhibitor of leukocyte-endothelial cell interactions that are mediated by either E- or L-selectin.

2/7/2 (Item 2 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11092707 BIOSIS Number: 97292707
Selectins in leukocyte extravasation: Function of a common epitope on L- and E-selectin
Jutila M A
Veterinary Molecular Biology, Montana State Univ., Bozeman, MT 59717, USA
0 (0). 1994. 235-262.
Full Journal Title: August, J. T., M. W. Anders and F. Murad (Ed.). Advances in Pharmacology, Vol. 25. xii+468p. Academic Press, Inc.: San Diego, California, USA; London, England, UK. ISBN 0-12-032925-5.
ISSN: 1054-3589
Language: ENGLISH
Print Number: Biological Abstracts/RRM Vol. 046 Iss. 007 Ref. 098060

2/7/3 (Item 3 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11076909 BIOSIS Number: 97276909
Survival in lung reperfusion injury is improved by an antibody that binds and inhibits L- and E-selectin
Steinberg J B; Mao H-Z; Niles S D; Jutila M A; Kapelanski D P
Div. Cardiothoracic Surg., UCSD Med. Cent., 225 Dickinson St., San Diego, CA 92103-8892, USA
Journal of Heart and Lung Transplantation 13 (2). 1994. 306-318.
Full Journal Title: Journal of Heart and Lung Transplantation
ISSN: 1053-2498
Language: ENGLISH
Print Number: Biological Abstracts Vol. 097 Iss. 012 Ref. 178459
The selectins are a three-member family of leukocyte, platelet, and endothelial cell adhesion proteins that mediate leukocyte traffic into normal and inflamed tissues. P-selectin is expressed by endothelial cells and platelets, E-selectin by endothelial cells, and L-selectin by

circulating leukocytes. To determine if selectin-mediated leukocyte adhesion influences the development of lung reperfusion injury, we studied hemodynamics and respiratory and inert gas exchange in sheep subjected to 3-hour in situ left lung ischemia followed by 6-hour left lung reperfusion with the right lung excluded. Ten minutes before reperfusion, eight animals received EL-246 (1 mg/kg intravenously), a novel antihuman selectin antibody that recognizes and blocks both L- and E-selectin and cross-reacts in sheep. Eight control animals with ischemia received no treatment, whereas three received an isotype-matched antihuman L-selectin antibody that does not cross-react in sheep (DREG-56, 1 mg/kg intravenously). Eight sham control sheep underwent an identical operative procedure but were never subjected to ischemia. Volume-cycled, pressure-limited (20 cm H-2O) mechanical ventilation was consistent in all animals throughout the experiment. Six-hour survival in EL-246 recipients (100%) was significantly higher than in either ischemic control sheep (37.5%) or DR-EG-56 recipients (33.3%), but gravimetric lung water was equivalent in EL-246 recipients (5.9 +- 1.7 ml/kg), ischemic control sheep (8.3 +- 3.0 ml/kg), and DREG-56 recipients (9.1 +- 2.6 ml/kg). Although inert gas shunt at 1/2 hour of reperfusion was no different when contrasted in EL-246 recipients (15% +- 8%), ischemic control sheep (30% +- 25%), and DREG-56 recipients (35% +- 21%), shunts in EL-246 recipients resolved (4% +- 4%) within the 6-hour study period and were associated with a concomitant improvement in respiratory gas exchange. Peripheral blood neutrophil counts increased after both EL-246 and DREG-56 administration, suggesting that the beneficial effect of EL-246 was not incurred by leukocyte depletion. We conclude that mechanisms other than activated neutrophils may account for the initial deterioration of respiratory gas exchange in lung reperfusion injury and inhibition of selectin function improves survival by preventing leukocyte-mediated amplification of this early process.

2/7/4 (Item 4 from file: 55)

9535279 BIOSIS Number: 94040279
CHARACTERIZATION OF A FUNCTIONALLY IMPORTANT AND EVOLUTIONARILY WELL-CONSERVED EPITOPE MAPPED TO THE SHORT CONSENSUS REPEATS OF E SELECTIN AND L SELECTIN

JUTILA M A; WATTS G; WALCHECK B; KANSAS G S
VETERINARY MOLECUALR BIOLOGY, MONTANA STATE UNIVERSITY, BOZEMAN, MT 59717.

J EXP MED 175 (6). 1992. 1565-1573. CODEN: JEMEA
Full Journal Title: Journal of Experimental Medicine
Language: ENGLISH

Selectins reperesent a new family of adhesion molecules, expressed by leukocytes and endothelial cells, that are involved in the regulation of leukocyte traffic. Here we have characterized a new monoclonal antibody (mAb) (EL-246) that recognizes both human leukocyte L-selectin (previously called LAM-1, LECAM-1, or gp90MEL-14) and endothelial cell E-selectin (previously called ELAM-1). EL-246 recognized a 110-kD protein expressed on cells transfected with E-selectin cDNA and stained many postcapillary venules in inflamed human tonsil. EL-246 also stained human peripheral blood leukocytes and showed identity with anti-L-selectin mAb in two-color flow cytometric analysis. The expression of the leukocyte EL-246 antigen was regulated in the same manner as L-selectin and EL-246 recognized anti-L-selectin mAb affinity-purified antigen in SDA/PAGE Western blot analysis. Further, L-selectin cDNA transfectants were specifically stained

by EL-246. EL-246 blocked >95% of lymphocyte adhesion to peripheral lymph node high endothelial venules and >90% of neutrophil adhesion to E-selectin transfectants. In addition to the EL-246 epitope being expressed on two different human selectins, it was detected on L-selectin from a variety of different animals. Interestingly domain mapping studies localized the EL-246 epitope to the short consensus repeat (SCR) domains of L-selectin. EL-246 is the first mAb that recognizes two different selectins and potentially defines a functional epitope encoded by the SCR domains. Inhibitors of selectin function targeted to this region would be expected to have the added advantage of simultaneously blocking the activity of two distinct of adhesion protein involved in inflammation.

```
?s (scr and selectin?)

          1387  SCR
         20127  SELECTIN?
      S3   20  (SCR AND SELECTIN?)
?s scr and selectin?

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         20127  SELECTIN?
      S4   20  SCR AND SELECTIN?
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?t s5/7/all


 5/7/1     (Item 1 from file: 55)
DIALOG(R)File  55:BIOSIS PREVIEWS(R)
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10993634     BIOSIS Number: 97193634
  Secondary combined resistance to the multidrug-resistance-reversing
activity of cyclosporin A in the cell line F4-6RADR-CsA
  Dietel M; Herzig I; Reymann A; Brandt I; Schaefer B; Bunge A; Heidebrecht
H-J; Seidel A
  Inst. Pathologie, Christian-Albrechts-Univ., Michaelisstr. 11, D-24105
Kiel, GER
  Journal of Cancer Research and Clinical Oncology 120 (5). 1994. 263-271.
  Full Journal Title: Journal of Cancer Research and Clinical Oncology
  ISSN: 0171-5216
  Language: ENGLISH
  Print Number: Biological Abstracts Vol. 097 Iss. 009 Ref. 127297
```

Multidrug-resistant tumor cells can be resensitized by combined application of the selecting cytostatic drug and a chemosensitizer, such as cyclosporin A (CsA) or a calcium channel blocker. Since clinical trials on the circumvention of multidrug resistance (MDR) with chemosensitizers report disparate results, we investigated whether tumor cells of the MDR phenotype can develop additional resistance to the cytostatic chemosensitizer combination. Thus, the Adriamycin(ADR)-selected, P-glycoprotein-positive MDR Friend leukemia cell line F4-6RADR was exposed to stepwise increased concentrations of CsA at a constant level of 0.05 mu-g/ml ADR. The initial CsA concentration (plus 0.05 mu-g/ml ADR) to inhibit cell growth of F4-6RADR cells by 50% (IC-50) was 0.04 mu-g/ml. By

continuous incubation for more than 6 months, the IC-50 for CsA (at constant ADR) was elevated to 3.6 mu-g/ml (90-fold), thus generating the variant F4-6RADR-CsA. The F4-6RADR-CsA cells were cross-resistant for cyclosporin H (CsH), a non-immunosuppressive derivative of CsA. As shown by immunocytochemistry as well as by the polymerase chain reaction and by Western blotting including densitometry, P-glycoprotein was preserved in the F4-6RADR-CsA variant and was expressed at a 4-fold higher level than in F4-6RADR cells. Sodium dodecyl sulfate/polyacrylamide gel electrophoresis analysis could detect no new proteins in F4-6RADR-CsA as compared to F4-6RADR. Interestingly, resistance of F4-6RADR-CsA cells remained reversible for the calcium antagonists verapamil and dihydropyridine B859-35 (dexniguldipine-HCl), indicating that CsA and these compounds interfere with the P glycoprotein function by different pharmacodynamic mechanisms. Transport studies with (14C)ADR, performed in the presence and absence of chemosensitizers, confirmed the good correlation of P-glycoprotein function with the pattern of resistance found in proliferation assays. Cellular accumulation of (3H)cyclosporin was reduced to 71% of that of the F4-6 controls in F4-6RADR-CsA cells, but remained at the level of controls in F4-6RADR cells. Results indicate that increased amounts of the P-glycoprotein - besides other, perhaps more important mechanisms that are as yet unknown partially mediate CsA resistance in F4-6RADR-CsA cells. We have designated this new form of resistance "secondary combined resistance" (SCR). The results suggest that at least some clinical cases of insensitivity to chemosensitizers or of relapse after reversing therapy could be explained by SCR, and that resensitizing treatment of tumor patients should be based on the consideration of several chemosensitizers of different pharmacodynamics.

5/7/2 (Item 2 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10967348 BIOSIS Number: 97167348
A role for the epidermal growth factor-like domain of P-selectin in ligand recognition and cell adhesion
Kansas G S; Saunders K B; Ley K; Zakrzewicz A; Gibson R M; Furie B C; Furie B; Tedder T F
Dep. Immunology, Box 3010, Duke University Medical Center, Durham, NC 27710, USA
Journal of Cell Biology 124 (4). 1994. 609-618.
Full Journal Title: Journal of Cell Biology
ISSN: 0021-9525
Language: ENGLISH
Print Number: Biological Abstracts Vol. 097 Iss. 008 Ref. 101018
The selectin family of adhesion molecules mediates the initial interactions of leukocytes with endothelium. The extracellular region of each selectin contains an amino-terminal C-type lectin domain, followed by an EGF-like domain and multiple short consensus repeat units (SCR). Previous studies have indirectly suggested a role for each of the extracellular domains of the selectins in cell adhesion. In this study, a panel of chimeric selecting created by exchange of domains between L- and P-selectin was used to directly examine the role of the extracellular domains in cell adhesion. Exchange of only the lectin domains between L- and P-selectin conferred the adhesive and ligand recognition functions of the lectin domain of the parent molecule. However, chimeric selectins which contained both the lectin domain of L-selectin and the EGF-like domain of P-selectin exhibited dual ligand-binding specificity. These chimeric

proteins supported adhesion both to myeloid cells and to high endothelial venules (HEV) of lymph nodes and mesenteric venules in vivo. Exchange of the SCR domains had no detectable effect on receptor function or specificity. Thus, the EGF-like domain of P-selectin may play a direct role in ligand recognition and leukocyte adhesion mediated by P-selectin, with the lectin plus EGF-like domains collectively forming a functional ligand recognition unit.

5/7/3 (Item 3 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10028445 BIOSIS Number: 95028445
MOLECULAR MECHANISM OF HEMOLYMPH CLOTTING SYSTEM IN LIMULUS
IWANAGA S; MIYATA T; TOKUNAGA F; MUTA T
DEP. BIOL., FAC. SCI., KYUSHU UNIV. 33, FUKUOKA 812, JPN.
THROMB RES 68 (1). 1992. 1-32. CODEN: THBRA
Full Journal Title: Thrombosis Research
Language: ENGLISH
Limulus (horseshoe crab) hemolymph is known to be very sensitive to bacterial endotoxin (LPS), which causes a rapid coagulation response. Hemolymph contains a single type of hemocyte that undergoes aggregation, adhesion, and degranulation in response to LPS. The granule contents are released into the hemolymph, where they form an insoluble gel. We have characterized four components invovled in this coagulation response that comprise a cascade of three serine protease zymogens (factor C, factor B, and proclotting enzyme) and one clottable protein (coagulogen). Of these components, factor C sensitive to LPs is a protein composed of five complement-related domains ("Sushi" or SCR), an EGF-like domain, and a C-type lectinlike domain as well as a putative amino-terminal LPS-binding domain. This domain structure is very similar to that of selectin family of cell adhesion molecules, suggesting that it might also function as a cell adhesion molecule after the release into the hemolymph. Factor B and the proclotting enzyme share a common Cys-rich motif ("cliplike" domain) in the amino-terminal portions. This domain is also found in a putative serine protease zymogen ("easter") in Drosophila, which is essential for normal embryonic development. All four of the components of the cascade and an antibacterial protein (anti-LPS factor) are localized to a specific type of the hemocyte granule. Another antibacterial peptide (tachyplesins I and II) is localized in a distinct granule population. The contents of both granule populations are released into the hemolympin in response to LPS, where they cooperate in immobilization and killing of Gram-negative bacteria.

5/7/4 (Item 4 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10011629 BIOSIS Number: 95011629
PREDICTING CHRONIC RENAL INSUFFICIENCY IN IDIOPATHIC MEMBRANOUS GLOMERULONEPHRITIS
PEI Y; CATTRAN D; GREENWOOD C
DIV. NEPHROL., TORONTO HOSP., 13 EN-228, 200 ELIZABETH ST., TORONTO, ONTARIO, CANADA M5G 2C4.
KIDNEY INT 42 (4). 1992. 960-966. CODEN: KDYIA
Full Journal Title: Kidney International
Language: ENGLISH

We developed an approach in quantifying the risk of developing chronic renal insufficiency (CRI) based on a cohort of 184 patients with idiopathic membranous glomerulonephritis (IMGN), prospectively followed by the Toronto [Canada] Glomerulonephritis Registry between 1974 and 1988. After a mean follow-up period of 5.8 years, 26% of patients developed CRI (defined as persistent reduction of creatinine clearance (CCr) .ltoreq. 60 ml/min/1.73 m2 for .gtoreq. 12 months). We found that when compared to the baseline probability of the unselected patients, the severity of proteinuria at kidney biopsy added only marginally to the prediction of CRI. We introduced a special test condition: persistent proteinuria (PP) (that is, duration of proteinuria, g/day, above different cut-off levels). We examined the positive predictive value (PPV) and sensitivity (SEN) of 15 arbitrarily chosen levels of PP (that is, proteinuria .gtoreq. 4, 6 or 8 g/day persisting for .gtoreq. 6, 9, 12, 18 or 24 months) to select levels with optimal predictive characteristics. We found that PP .gtoreq. 8 g/day for .gtoreq. six months was a simple and useful predictor of CRI with a PPV and SEN of 66%. To further improve our prediction, we tested the following parameters: age, sex, initial SCr and CCr, proteinuria, serum albumin, hypertension, rate of change of CCr over time, and therapy (steroids .+-. immunosuppressive drugs) in a multivariate analysis. Proteinuria, initial CCr, and rate of change of CCr were most important in predicting CRI. Fifteen models were then developed by including each patient's CCr at the start of PP and its rate of change during the time period selected. Two models based on PP .gtoreq. 4 g/day for .gtoreq. 18 months, or .gtoreq. 6 g/day for .gtoreq. 9 months significantly improved the PPV's for CRI from those based on the same levels of PP alone. Using these test conditions, we can improve the prediction of CRI from a baseline probability of 26% in unselected patients to a range of 55 to 86% in the "high-risk" patients (with SEN > 60%). Application of these predictive strategies in IMGN will be useful in managing the individual patients and in selecting patients for clinical trials by limiting the exposure of potentially toxic therapy to the "high-risk" patients.

5/7/5 (Item 5 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

9535279 BIOSIS Number: 94040279
CHARACTERIZATION OF A FUNCTIONALLY IMPORTANT AND EVOLUTIONARILY WELL-CONSERVED EPITOPE MAPPED TO THE SHORT CONSENSUS REPEATS OF E SELECTIN AND L SELECTIN
JUTILA M A; WATTS G; WALCHECK B; KANSAS G S
VETERINARY MOLECUALR BIOLOGY, MONTANA STATE UNIVERSITY, BOZEMAN, MT 59717.
J EXP MED 175 (6). 1992. 1565-1573. CODEN: JEMEA
Full Journal Title: Journal of Experimental Medicine
Language: ENGLISH
Selectins reperesent a new family of adhesion molecules, expressed by leukocytes and endothelial cells, that are involved in the regulation of leukocyte traffic. Here we have characterized a new monoclonal antibody (mAb) (EL-246) that recognizes both human leukocyte L-selectin (previously called LAM-1, LECAM-1, or gp90MEL-14) and endothelial cell E-selectin (previously called ELAM-1). EL-246 recognized a 110-kD protein expressed on cells transfected with E-selectin cDNA and stained many postcapillary venules in inflamed human tonsil. EL-246 also stained human peripheral blood leukocytes and showed identity with anti-L-selectin mAb in two-color flow cytometric analysis. The expression of the leukocyte EL-246 antigen

was regulated in the same manner as L-selectin and EL-246 recognized anti-L-selectin mAb affinity-purified antigen in SDA/PAGE Western blot analysis. Further, L-selectin cDNA transfectants were specifically stained by EL-246. EL-246 blocked >95% of lymphocyte adhesion to peripheral lymph node high endothelial venules and >90% of neutrophil adhesion to E-selectin transfectants. In addition to the EL-246 epitope being expressed on two different human selectins, it was detected on L-selectin from a variety of different animals. Interestingly domain mapping studies localized the EL-246 epitope to the short consensus repeat (SCR) domains of L-selectin. EL-246 is the first mAb that recognizes two different selectins and potentially defines a functional epitope encoded by the SCR domains. Inhibitors of selectin function targeted to this region would be expected to have the added advantage of simultaneously blocking the activity of two distinct of adhesion protein involved in inflammation.

5/7/6 (Item 6 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

9523578 BIOSIS Number: 94028578
STRUCTURE AND FUNCTION OF L SELECTIN REVIEW ARTICLE
KANSAS G S
DEP. PATHOL., HARVARD MED. SCH., BOSTON, MASS.
APMIS (ACTA PATHOL MICROBIOL IMMUNOL SCAND) 100 (4). 1992. 287-293.
CODEN: APMSE
Full Journal Title: APMIS (Acta Pathologica Microbiologica et Immunologica Scandinavica)
Language: ENGLISH
The selectins are a newly described family of carbohydrate-binding adhesion molecules involved in the regulation of leukocyte traffic. Selectins are composed of an N-terminal C-type lectin domain, a single EGF domain, a variable number of short concensus repeat (SCR) domains, a transmembrane region and a cytoplasmic tail. L-selectin (LAM-1/LECAM-1/LECCAM-1) is the only selectin expressed on leukocytes, and mediates a number of leukocyte-endothelial interactions, including the binding of lymphocytes to HEV of peripheral lymph node high endothelial venules (HEV), neutrophil rolling, and leukocyte attachment to cytokine-treated endothelium in vitro. Stable transfectants expressing a series of chimeric selectins and deletion mutants were functionally analyzed in order to determine the molecular basis of adhesion mediated by L-selectin. The specificity of adhesion was found to reside entirely within the lectin domain, suggesting that this domain is the only domain of the protein to interact with the carbohydrate ligand. These results make previous observations that certain mAbs which block function map to each of the extracellular domains difficult to interpret. In addition, deletion of the cytoplasmic tail of L-selectin abolished adhesion, without affecting ligand recognition. Thus, each domain of the selectins has an important, but distinct, role in cell adhesion.

5/7/7 (Item 7 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

5947979 BIOSIS Number: 84080544
ELECTRODERMAL RESPONDING AND CHLORPROMAZINE TREATMENT IN SCHIZOPHRENIA
YANNITSI S; LIAKOS A; PAPAKOSTAS Y

DEP. PSYCHIATRY, IOANNINA UNIV., MED. SCH., IOANNINA 453 32, GREECE.
BR J PSYCHIATRY 150 (JUNE). 1987. 850-853. CODEN: BJPYA
Full Journal Title: British Journal of Psychiatry
Language: ENGLISH

Skin conductance level (SCL) and skin conductance responses (SCR) to a random series of tones were measured in 25 drug-free schizophrenic patients, 15 male and 10 female, before and after standard chlorpromazine treatment. The DSM-III diagnostic criteria were used for selecting subjects. Psychopathology was measured with the Brief Psychiatric Rating Scale. After treatment, patients showed an improved psychopathology and decreased SCL. There was a transition of patients to lower response categories: the number of responders decreased twice and the number of non-responders increased three times. Responders exhibited significantly higher SCL than non-responders and fast habituators were between the two groups.

5/7/8 (Item 1 from file: 72)
DIALOG(R)File 72:EMBASE

9145184 EMBASE No: 94083655
Analysis of unresolved chromatograms by the absorbance ratio and sequential chromatogram ratio techniques coupled with peak suppression
Bahowick T.J.; Dunphy D.R.; Synovec R.E.
Department of Chemistry, University of Washington, Seattle, WA 98195 USA
J. CHROMATOGR. A (Netherlands) , 1994, 663/2 (135-150) CODEN: JCRAE
ISSN: 0021-9673
LANGUAGES: English SUMMARY LANGUAGES: English

The sequential chromatogram ratio (SCR) technique was successively applied or was coupled with the absorbance ratio (AR) technique to facilitate analysis of a peak of interest that was overlapped with two other peaks. First, the AR or SCR technique was used to suppress one undesired peak. This created or elongated a region of pure-component elution for the peak of interest. Then the appropriate ratio technique was applied to this region for qualitative and quantitative analysis. The AR technique allows suppression and qualitative analysis of unknown components via the absorptivity ratio. For the SCR technique, peak identity can be deduced prior to suppression and quantitative analysis. A statistical peak matching procedure that employs user-selected standards is described for the SCR technique, by which components in sequentially injected samples may be identified based on differences in retention time, t(R), or in diffusion coefficient, D(m), which controls peak width. For two similarly retained analytes in sequentially injected samples, having a factor-of-two difference in D(m), the problem of reduced resolution, R(s) with a third peak was investigated by manipulating the data to simulate a reduction in selectivity factor. Below a limit, R(s) = 0.38, the original two analytes could no longer be qualitatively distinguished. At this same R(s) limit, the two-times difference in D(m), for two analytes having essentially zero t(R)-based resolution, provided equivalent qualitative discrimination of peaks as a t(R)-based resolution of 0.12 for two analytes having equal D(m), The classical problems of inaccurate baseline correction and run-to-run retention variation were examined, and the latter was more limiting for the SCR technique. Still, small t(R) shifts were adequately corrected by selecting and aligning a common peak in sequential chromatograms.

5/7/9 (Item 2 from file: 72)
DIALOG(R)File 72:EMBASE

8488075 EMBASE No: 92163085
Structure and function of L-selectin
Kansas G.S.
Department of Pathology, Harvard Medical School, Boston, MA USA
APMIS (Denmark) , 1992, 100/4 (287-293) CODEN: APMSE ISSN: 0903-4641
ADONIS ORDER NUMBER: 090346419200053X
LANGUAGES: English SUMMARY LANGUAGES: English
The selectins are a newly described family of carbohydrate-binding adhesion molecules involved in the regulation of leukocyte traffic. Selectins are composed of an N-terminal C-type lectin domain, a single EGF domain, a variable number of short consensus repeat (SCR) domains, a transmembrane region and a cytoplasmic tail. L-selectin (LAM-1/LECAM-1/LECCAM-1) is the only selectin expressed on leukocytes, and mediates a number of leukocyte-endothelial interactions, including the binding of lymphocytes to HEV of peripheral lymph node high endothelial venules (HEV), neutrophil rolling, and leukocyte attachment to cytokine-treated endothelium in vitro. Stable transfectants expressing a series of chimeric seletins and deletion mutants were functionally analyzed in order to determine the molecular basis of adhesion mediated by L-selectin. The specificity of adhesion was found to reside entirely within the lectin domain, suggesting that this domain is the only domain of the protein to interact with the carbohydrate ligand. These results make previous observations that certain mAbs which block function map to each of the extracellular domains difficult to interpret. In addition, deletion of the cytoplasmic tail of L-selectin abolished adhesion, without affecting ligand recognition. Thus, each domain of the selectins has an important but distinct role in cell adhesion.
?s (short(w)consensus(w)repeat) and selectin?

```
          434958  SHORT
           34290  CONSENSUS
           54861  REPEAT
             205  SHORT(W)CONSENSUS(W)REPEAT
           20127  SELECTIN?
      S6      16  (SHORT(W)CONSENSUS(W)REPEAT) AND SELECTIN?
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?ds

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Set     Items   Description
S1         10   EL(W)246 AND SELECTIN?
S2          4   RD S1 (unique items)
S3         20   (SCR AND SELECTIN?)
S4         20   SCR AND SELECTIN?
S5          9   RD S4 (unique items)
S6         16   (SHORT(W)CONSENSUS(W)REPEAT) AND SELECTIN?
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?s s4 and s6

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             20  S4
             16  S6
      S7      8  S4 AND S6
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?rd s7

...completed examining records

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      S8      3  RD S7 (unique items)
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?s s4 or s6 rd

>>>Term "RD" in invalid position
?s s4 or s6

	20	S4
	16	S6
S9	28	S4 OR S6

?rd s9

...completed examining records

S10	13	RD S9 (unique items)

?t s10/3/all

10/3/1 (Item 1 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

11128707 BIOSIS Number: 97328707
In vivo and in vitro functional examination of a conserved epitope of L- and E-selectin crucial for leukocyte-endothelial cell interactions
Bargatze R F; Kurk S; Watts G; Kishimoto T K; Speer C A; Jutila M A
Veterinary Mol. Biol. Lab., Montana State University, Bozeman, MT 59717, USA
Journal of Immunology 152 (12). 1994. 5814-5825.
Full Journal Title: Journal of Immunology
ISSN: 0022-1767
Language: ENGLISH
Print Number: Biological Abstracts Vol. 098 Iss. 003 Ref. 035219

10/3/2 (Item 2 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10993634 BIOSIS Number: 97193634
Secondary combined resistance to the multidrug-resistance-reversing activity of cyclosporin A in the cell line F4-6RADR-CsA
Dietel M; Herzig I; Reymann A; Brandt I; Schaefer B; Bunge A; Heidebrecht H-J; Seidel A
Inst. Pathologie, Christian-Albrechts-Univ., Michaelisstr. 11, D-24105 Kiel, GER
Journal of Cancer Research and Clinical Oncology 120 (5). 1994. 263-271.
Full Journal Title: Journal of Cancer Research and Clinical Oncology
ISSN: 0171-5216
Language: ENGLISH
Print Number: Biological Abstracts Vol. 097 Iss. 009 Ref. 127297

10/3/3 (Item 3 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10967348 BIOSIS Number: 97167348
A role for the epidermal growth factor-like domain of P-selectin in ligand recognition and cell adhesion
Kansas G S; Saunders K B; Ley K; Zakrzewicz A; Gibson R M; Furie B C;

Furie B; Tedder T F
Dep. Immunology, Box 3010, Duke University Medical Center, Durham, NC 27710, USA
Journal of Cell Biology 124 (4). 1994. 609-618.
Full Journal Title: Journal of Cell Biology
ISSN: 0021-9525
Language: ENGLISH
Print Number: Biological Abstracts Vol. 097 Iss. 008 Ref. 101018

10/3/4 (Item 4 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10964617 BIOSIS Number: 97164617
Molecular basis for L-selectin function in comparison with P- and E-selectin
Tedder T F; Saunders K B; Kansas G S; Ley K; Zakrzewicz A; Gibson R M; Furie B C; Furie B
Duke Univ. Med. Center, Durham, NC 27710, USA
Journal of Cellular Biochemistry Supplement 0 (18 PART A). 1994. 261.
Full Journal Title: Keystone Symposium on Inflammation, Growth Regulatory Molecules and Atherosclerosis, Keystone, Colorado, USA, January 16-23, 1994. Journal of Cellular Biochemistry Supplement
ISSN: 0733-1959
Language: ENGLISH
Document Type: CONFERENCE PROCEEDINGS
Print Number: Biological Abstracts/RRM Vol. 046 Iss. 004 Ref. 061218

10/3/5 (Item 5 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10028445 BIOSIS Number: 95028445
MOLECULAR MECHANISM OF HEMOLYMPH CLOTTING SYSTEM IN LIMULUS
IWANAGA S; MIYATA T; TOKUNAGA F; MUTA T
DEP. BIOL., FAC. SCI., KYUSHU UNIV. 33, FUKUOKA 812, JPN.
THROMB RES 68 (1). 1992. 1-32. CODEN: THBRA
Full Journal Title: Thrombosis Research
Language: ENGLISH

10/3/6 (Item 6 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10011629 BIOSIS Number: 95011629
PREDICTING CHRONIC RENAL INSUFFICIENCY IN IDIOPATHIC MEMBRANOUS GLOMERULONEPHRITIS
PEI Y; CATTRAN D; GREENWOOD C
DIV. NEPHROL., TORONTO HOSP., 13 EN-228, 200 ELIZABETH ST., TORONTO, ONTARIO, CANADA M5G 2C4.
KIDNEY INT 42 (4). 1992. 960-966. CODEN: KDYIA
Full Journal Title: Kidney International
Language: ENGLISH

10/3/7 (Item 7 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

9535279 BIOSIS Number: 94040279
CHARACTERIZATION OF A FUNCTIONALLY IMPORTANT AND EVOLUTIONARILY WELL-CONSERVED EPITOPE MAPPED TO THE SHORT CONSENSUS REPEATS OF E SELECTIN AND L SELECTIN
JUTILA M A; WATTS G; WALCHECK B; KANSAS G S
VETERINARY MOLECUALR BIOLOGY, MONTANA STATE UNIVERSITY, BOZEMAN, MT 59717.
J EXP MED 175 (6). 1992. 1565-1573. CODEN: JEMEA
Full Journal Title: Journal of Experimental Medicine
Language: ENGLISH

10/3/8 (Item 8 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

9523578 BIOSIS Number: 94028578
STRUCTURE AND FUNCTION OF L SELECTIN REVIEW ARTICLE
KANSAS G S
DEP. PATHOL., HARVARD MED. SCH., BOSTON, MASS.
APMIS (ACTA PATHOL MICROBIOL IMMUNOL SCAND) 100 (4). 1992. 287-293. CODEN: APMSE
Full Journal Title: APMIS (Acta Pathologica Microbiologica et Immunologica Scandinavica)
Language: ENGLISH

10/3/9 (Item 9 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

9508134 BIOSIS Number: 94013134
GLYCOBIOLOGY AND BLOOD CELLS
NEEL D; AUBERY M; DERAPPE C
FAC. DE MED., 45 RUE DES SAINTS-PERES, 75006 PARIS, FR.
M-S (MED SCI) 8 (3). 1992. 233-238. CODEN: MSMSE
Full Journal Title: M-S (Medecine Sciences)
Language: FRENCH

10/3/10 (Item 10 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

7660194 BIOSIS Number: 90028194
STRUCTURE OF THE GENE ENCODING THE HUMAN LEUKOCYTE ADHESION MOLECULE-1 TQ1 LEU-8 OF LYMPHOCYTES AND NEUTROPHILS
ORD D C; ERNST T J; ZHOU L-J; RAMBALDI A; SPERTINI O; GRIFFIN J; TEDDER T F
DIV. TUMOR IMMUNOL., DANA-FARBER CANCER INST., 44 BINNEY ST., BOSTON, MASS. 02115.
J BIOL CHEM 265 (14). 1990. 7760-7767. CODEN: JBCHA
Full Journal Title: Journal of Biological Chemistry
Language: ENGLISH

10/3/11 (Item 11 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

5947979 BIOSIS Number: 84080544
ELECTRODERMAL RESPONDING AND CHLORPROMAZINE TREATMENT IN SCHIZOPHRENIA
YANNITSI S; LIAKOS A; PAPAKOSTAS Y
DEP. PSYCHIATRY, IOANNINA UNIV., MED. SCH., IOANNINA 453 32, GREECE.
BR J PSYCHIATRY 150 (JUNE). 1987. 850-853. CODEN: BJPYA
Full Journal Title: British Journal of Psychiatry
Language: ENGLISH

10/3/12 (Item 1 from file: 72)
DIALOG(R)File 72:EMBASE

9145184 EMBASE No: 94083655
Analysis of unresolved chromatograms by the absorbance ratio and sequential chromatogram ratio techniques coupled with peak suppression
Bahowick T.J.; Dunphy D.R.; Synovec R.E.
Department of Chemistry, University of Washington, Seattle, WA 98195 USA
J. CHROMATOGR. A (Netherlands) , 1994, 663/2 (135-150) CODEN: JCRAE
ISSN: 0021-9673
LANGUAGES: English SUMMARY LANGUAGES: English

10/3/13 (Item 2 from file: 72)
DIALOG(R)File 72:EMBASE

8488075 EMBASE No: 92163085
Structure and function of L-selectin
Kansas G.S.
Department of Pathology, Harvard Medical School, Boston, MA USA
APMIS (Denmark) , 1992, 100/4 (287-293) CODEN: APMSE ISSN: 0903-4641
ADONIS ORDER NUMBER: 090346419200053X
LANGUAGES: English SUMMARY LANGUAGES: English

?s raf and ige

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          3725  RAF
         33028  IGE
    S11     2  RAF AND IGE
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?t s11/3/all

11/3/1 (Item 1 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)

10513632 BIOSIS Number: 96113632
SIGNIFICANCE OF ELEVATED SERUM SQUAMOUS CELL CARCINOMA SCC-RELATED ANTIGEN AND LACTATE DEHYDROGENASE LDH LEVELS IN SENILE ERYTHRODERMA FOLLOWING ECZEMA
TSUKAHARA T; OTOYAMA K; HORIUCHI Y
DEP. DERMATOLOGY, KITASATO UNIV. SCH. MED., SAGAMIHARA 228, JPN.

J DERMATOL (TOKYO) 20 (6). 1993. 346-350. CODEN: JDMYA
Full Journal Title: Journal of Dermatology (Tokyo)
Language: ENGLISH

11/3/2 (Item 1 from file: 399)
DIALOG(R)File 399:CA Search(R)

110006077 CA: 110(1)6077s JOURNAL
V-raf converts E.mu.-myc B cells into macrophages
AUTHOR(S): Klinken, S. Peter; Alexander, Warren S.; Cockerill, Peter; Adams, Jerry M.
LOCATION: Walter and Eliza Hall Inst. Med. Res., R. Melbourne Hosp., Victoria, 3050, Australia
JOURNAL: UCLA Symp. Mol. Cell. Biol., New Ser. DATE: 1988 VOLUME: 85
NUMBER: B Cell Dev. PAGES: 271-82 CODEN: USMBD6 ISSN: 0735-9543
LANGUAGE: English
?

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=>
=>
=> s transgenic
L17         838 TRANSGENIC
=> s l17 and antigen?
          19154 ANTIGEN?
L18         355 L17 AND ANTIGEN?
=> s l18 and (mouse or nonhuman)
          27385 MOUSE
            394 NONHUMAN
L19         251 L18 AND (MOUSE OR NONHUMAN)
=> s l19 and (antibod? or immunoglobulin?)
          22248 ANTIBOD?
           6664 IMMUNOGLOBULIN?
L20         234 L19 AND (ANTIBOD? OR IMMUNOGLOBULIN?)
=> s l20 and variable(w)region
         290677 VARIABLE
         365783 REGION

            656 VARIABLE(W)REGION
L21          23 L20 AND VARIABLE(W)REGION
=> s l21 and human(2w)variable(2w)region
         142704 HUMAN
         290677 VARIABLE
         365783 REGION
             25 HUMAN(2W)VARIABLE(2W)REGION
L22           7 L21 AND HUMAN(2W)VARIABLE(2W)REGION
=> d l22 1-7 cit

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